A CLINICAL STUDY ON DISCOID LUPUS ERYTHEMATOSUS

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CERTIFICATE

This is to certify that this dissertation entitled **'A CLINICAL STUDY ON DISCOID LUPUS ERYTHEMATOSUS'** submitted by **Dr. SUDHA. R** to The Tamil Nadu Dr. M.G.R. Medical University, Chennai is in partial fulfillment of the requirement for the award of **M.D., [DERMATO VENEREO LEPROLOGY]** and is a bonafide research work carried out by her under direct supervision and guidance.

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DECLARATION

I, **Dr.SUDHA. R** solemnly declare that I carried out this work on '**A CLINICAL STUDY ON DISCOID LUPUS ERYTHEMATOSUS'** at Department Of Dermatology, Government Rajaji Hospital during the period of Oct. 2010 – Sep. 2012. I also declared this bonafide work or a part of this work was not submitted by me or any other for any award, degree and diploma to any university, board either in India or abroad. This is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the rules and regulation for M.D.,[D.V.L] Degree examination.

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CONTENTS

ABBREVIATIONS

LE	-	Lupus Erythematosus
CLE	-	Cutaneous lupus erythematosus
DLE	-	Discoid lupus Erythematosus
SCLE	-	Subacute cutaneous lupus Erythematosus
SLE	-	Systemic lupus Erythematosus
MHC	-	Major Histocompatibility Complex
HLA	-	Human Leukocyte Antigen
IFN	-	interferon
TNF	-	tumor necrosis factor
GST-M1	-	Glutathione S-Transferase Mu1
IL	-	Interleukin
TCR	-	T cell receptor
ICAM-1	-	Intercellular Adhesion Molecule-1
TGF	-	Transforming growth factor
TLR	-	Toll like receptor
DC	-	Dendritic cell
LEP	-	LE Panniculitis
LET	-	Tumid lupus Erythematosus
ANA	-	Anti nuclear antibody
ACR	-	American college of rheumatology

INTRODUCTION

Discoid lupus Erythematosus (DLE) is a chronic disfiguring inflammatory skin disease. It is the most common form of cutaneous lupus erythematosus. It is characterized by erythematous indurated well defined scaly plaques of variable size, that resolve with atrophy, scarring and pigmentary changes. Follicular involvement is a prominent feature in DLE. Since there are only few published studies on DLE reported from India, a complete clinical profile of DLE patients was studied here.

Lupus Erythematosus (LE) is a multisystem autoimmune disorder. Professor James Gilliam classified cutaneous lesions of LE as specific and non-specific based on the characteristic histological changes.

The word ‘lupus’ means ‘wolf’ in Latin reminding the destructive injuries in the disease to the bite of the animal.

Cutaneous involvement is the second common clinical manifestation in LE next to joints. Among the LE specific skin lesions, DLE rarely manifests with systemic disease. Although discoid cutaneous lesions are typical of DLE, they are also seen in as many as 14% of the patients with systemic lupus erythematosus (SLE).

DLE is worldwide in distribution affecting frequently black people. The disease has a characteristic age and sex pattern, affecting individuals between 20-40 years of age with female preponderance.

The etio-pathogenesis of cutaneous lupus erythematosus (CLE) is thought to be related to the same autoimmune abnormality responsible for the systemic components of LE. The key feature in the pathogenesis is up regulation of the interferon-α (IFN-α) signaling.

Depending on the extent of the lesion involvement, DLE is classified as localized and disseminated type.

DLE lesions show characteristic histological features. Characteristic staining patterns are observed in the serological ANA-IFA testing and in the immunofluorescence study of the lesion.

Treatment options are based on the extent and severity of the disease. Sun-protection was advised for all patients and is advised to wear a broad-brimmed hat, protective clothes and to avoid short-sleeved shirts. Frequent sunscreen application, potent topical steroids, oral antimalarials, oral prednisolone are found to be useful.

REVIEW OF LITERATURE

HISTORICAL ASPECTS

- Laurent Theodore Biett of Paris first described Lupus Erythematosus as Erythema centrifugum and was reported by his student Cazenave in 1833[1].
- Biett's student Pierre Louis Alphee Cazenave renamed erythema centrifugum and coined the term Lupus Erythematosus in 1851[1, 2].
- In 1866, Ferdinand Von Hebra used the metaphor of a butterfly to describe malar rash [3].
- In 1872, Moriz Kaposi first described the systemic features of the disorder.
- In 1872, Kaposi described the exclusively cutaneous form of the disease as discoidal lupus [1].
- Sir William Osler coined the term systemic lupus erythematosus.
- Jonathan Hutchinson described the photosensitive nature.
- In 1948, Hematologist Malcolm Hargraves discovered the LE cell [4].
- In 1958, George Friou, demonstrated Anti nuclear factor [5].

- In 1955, Moore ad Lutz described the phenomenon of biological false positive VDRL in Lupus patients.

- Leonardt, Arnett and Schulman described familial aggregation of lupus [6].

- In 1954, Drug induced lupus was first described.

- In 1894 Payne first reported the use of quinine in the treatment of lupus erythematosus [7].

- In 1951, quinacrine was the first antimalarial to be used in the treatment of DLE.

EPIDEMIOLOGY OF DISCOID LUPUS ERYTHEMATOSUS (DLE)

INCIDENCE

The exact incidence and prevalence of DLE are unknown; DLE is responsible for 50 – 85% of cutaneous lupus erythematosus. Incidence of cutaneous LE is equal to that of SLE. [8] The incidence of DLE in one study was 3.56 per 100 000 persons: 1.04 per 100 000 for the generalized form and 2.52 per 100 000 for the localized form [8]

AGE

DLE is most common in individuals between 20 and 40 years of age. [9] But it can occur at any age. Cases have been reported in less than 15 years of age and in elderly over 70 years of age. [10]

SEX

DLE has a female preponderance. Female to male sex ratio was found to be 3: 2 to 3: 1. [9] Age of onset was slightly later in males when compared to females [11]

RACE

All races are affected. But the prevalence rate was higher in black race (African Americans) [9]

ETIO – PATHOGENESIS OF DLE

The pathogenesis of LE-specific skin lesion is inextricably intertwined with SLE pathogenesis. [9] Etio - pathogenesis is believed to be due to the interaction between genetic, environmental and retroviral factors resulting in loss of self tolerance.

Susceptibility Phase [9]				
1 HLA Genes	2. Complement Genes	3. Hormones		4. TNF genes
↓				
Induction Phase				
Viruses	UV radiation	Drugs	Tobacco	Apoptosis
Antigen Processing by DCs				
↓ **Expansion phase**				
	B cell proliferation	Auto Antibody formation	T – cell expansion	
↓				
	Cytotoxic T cells	**Injury phase**	Immune complexes	

SUSCEPTIBLE GENES

Genes of class I encode HLA A, B, Cw, those of class II encode HLA DP, DQ, DR, and those of class III encode molecules like components of complement C4A,B, C2, TNF, and heat shock proteins, (HSP)[13]

HLA Associations:

1. HLA Association in DLE shows increased susceptibility with HLA-B7,-B8 among class I MHC. HLA-DR2, -DR3, -DQA0102 among class II MHC [9]

   Other haplotypes with increased susceptibility to DLE are $A^{*}03$, $B^{*}07$, $DRB1^{*}15$ [12]

Complement deficiencies:

2. Inherited deficiencies of C2 & C4 complement components have been strongly linked to DLE. There is partial deficiency of both C4 allotypes in lupus panniculitis. [13] These complement deficiencies may cause failure to clear immune complexes and apoptotic cells. Increased numbers of apoptotic cells due to increased formation or reduced clearance, in turn lead to immunologic stimulation and finally to increased anti-Ro formation [13]

TNF genes and Heat shock proteins genes:

3. TNF genes & heat shock proteins genes that belong to class III MHC exacerbates cutaneous lupus erythematosus after UV radiation exposure, the pathogenic mechanism being translocation of intracellular and intranuclear antigens and their exposure to the immune system. [14]

Familial cases of DLE were found in 4% in one series. [15]

Genes outside MHC:

4. Genes outside MHC that could be associated with the susceptibility to cutaneous LE lesions are :

a) Genes encoding cytokines (IL-1, IL-10) and their receptors (Fc γRII, TCR),

b) Adhesion molecules (ICAM-1, E-Selectin),

c) Antioxidant enzymes (GST-Ml) and

d) Apoptosis genes (fas). [13]

Human Endogenous Retroviruses:

HERVs (Human Endogenous Retroviruses) that have originated from exogenous retrovirus, have integrated in to genome. [13] They are

transmitted genetically and are replication defective. [13] HERVs can lead to auto immunity directly by encoding auto antigens, or indirectly by affecting the expression of gene-regulating immune responses and tolerance. [16]

Induction phase (or) induction by environmental factors

Ultraviolet Radiation

UV radiation (both UVA and UVB) is the most important inducing factor of systemic manifestation of LE and LE specific skin disease.

1. UV radiation **induce apoptosis of keratinocytes** there by making cryptic peptides available for immunosurveillance[17] (i.e.) it results in translocation of nuclear antigens Ro, La, and calreticulin, from its normal locations inside epidermal keratinocytes to the cell surface.[17]

2. UVB radiation **induces release of CCL27** (cutaneous T cell - attracting chemokine) which up regulate expression of chemokine that in turn activate auto reactive T cells & IFN-α producing Dendritic cells.[18]

Drugs

Drugs induce lupus erythematosus by the following mechanisms.

1. Drugs that produce hypomethylation of DNA in turn will increase the activity of auto reactive lymphocytes.[9]

2. Photosensitizing drugs like UV radiation induce apoptosis of keratinocytes, translocation of nuclear antigens resulting in enhanced production of proinflammatory cytokines like TNF-α, IFN-α. [19]

Drugs that induce DLE lesions are isoniazid, D-penicillamine, and griseofulvin. [20] [21] [22]

Positive ANA, musculoskeletal symptoms and serositis are the predominant clinical presentation in drug induced LE [153] 25% of hydralazine induced and less than 5% of procinamide induced LE patients showed features of skin changes [153] Anti histone auto antibody represent the serologic marker in drug induced LE/ANA[153]

Drugs like hydrochlorothiazide, diltiazem, griseofulvin, terbinafine induce subacute cutaneous lupus erythematosus (SCLE) lesions and anti-Ro auto antibody. [153]

Anti TNF-α inhibitor induced lupus have skin manifestations including malar rash, SCLE, DLE, photosensitivity and purpura. [152] ANA and anti-ds DNA are predominant antibodies and not anti histone antibodies with the TNF-α blockers. [151]

Viruses

The antibodies to reovirus RNA found in 42% of patients suggest that viruses may have a pathogenic role in DLE. [20] DLE occurring at small pox vaccination scar [23] and herpes zoster scar [24] speculate the role of viruses as inducing factor in CLE.

Epstein – Barr virus (EBV) induces SLE by the following mechanisms

1) Molecular mimicry [25]

2) Through aberrant activation of TLR-7[26] and

3) By impaired EBV-specific T-cell response and increased levels of EBV-directed antibodies [27]

Tobacco Exposure

Lipogenic aromatic amines in tobacco smoke suggest increased frequency of DLE in smokers. [9] Smoking also has an impact on management. Smokers are less responsive to antimalarial treatment.[28] [29] [30]

Antigen Processing Dendritic cells

Dendritic cells are monocyte derived cell; exist as myeloid dendritic cell and plasmacytoid dendritic cell.

In normal individuals, in the absence of inflammation, the immature dendritic cells act as housekeepers and maintain peripheral tolerance to self antigens. [9]

In the background of genetic susceptibility and inducing factors like microbial exposure and inflammation, apoptosis occurs. The self antigens exposed after apoptosis are presented by mature dendritic cell to naive T cell in draining lymph node resulting in T cell & B cell activation with subsequent launching of an adaptive immune response.[31]

Plasmacytoid dendritic cell in lymphoid organs, on exposure to viral and bacterial pathogens produce IFN-α. Elevated IFN scores were reported in DLE and SCLE [32] that confirms the pathogenetic role of IFN-α. IFN-α activate myeloid dendritic cell to capture circulating apoptotic cells and present self-antigens to auto reactive CD4 T cells and also support B-cell proliferation and differentiation, leading to the clinical expression of LE. [33]

Role of complement:

Normally, complement proteins bind to apoptotic cells, which are then disposed of by "housekeeping" macrophages. [9] High risk for SLE is conferred by homozygous deficiencies of early complement components or their inhibitors, including C2 and C4 within the HLA gene complex and non-HLA C1q, 1r and C1-INH. [34] [35] [36][37] When complement proteins are deficient (a common characteristic of patients with lupus) and when they are not present on apoptotic cells, the apoptotic cells are recognized by dendritic cells (DCs) that are able to stimulate the adaptive immune response [9]

Role of inflammatory cytokines

1. Central to the pathogenesis is up regulation of the interferon-α (IFN-α) signaling. [38]

2. Up regulation of IFN – inducible antiviral protein Myxovirus–A. [38]

3. TNF-α produced by keratinocytes on exposure to UV radiation

   a) Induce apoptosis

   b) Release proinflammatory cytokines through NF-κβ and

c) Stimulates adaptive immune response by inducing HLA-DR expression. [9]

Both TNF-α and Anti-TNF therapies like etanarcept and infliximab results in the development or worsening of LE. TNF-α regulates IFN-α production in vitro by inhibiting the generation plasmacytoid DCs. [39] Thus over expression of IFN-α is thought to be a key event in immune dysregulation in lupus. [9]

4. Strong expression of TNF-related apoptosis-inducing ligand (TRAIL) in skin and blood. [41]

5. Interleukin (IL)-18 and the over expression of IL-18 receptor in keratinocytes was found to induce the apoptosis of keratinocytes via increased tumor necrosis factor (TNF)-α and decreased IL-12 production [40]

6. Some CLE patients showed increased IL-17 levels [40]

7. Down regulation of TGF-β, IL – 10 was observed in DLE patients [42]

Role of Toll like Receptors (TLRs)

Stimulation of TLRs by circulating DNA, anti DNA complexes induces proliferation of auto reactive B cells and IFN-α production by

dendritic cells. [9] Members in the TLR7/TLR8/TLR9 activation pathways are candidate genes for increased risk of the generation of auto antibodies to nuclear complexes that are found in SLE patients [43]

Thus blocking TLRs may have therapeutic implications in lupus. [9]

Expansion and Injury phase

T Cells

T cells mediating a key role in induction and expansion phases are involved in both central and peripheral tolerance.[9]

Self antigen presentation by DCs to auto reactive T cells leads to T cell activation which in turn activates auto reactive B cells to produce auto antibodies.

A pan -T cell dysfunction seems to exist in SLE, which is characterized by exaggerated helper and diminished regulatory / suppressor CD4+CD25+ and CD8+ T cell activities.[44] Cytotoxic T lymphocytes mediate tissue damage in SLE and in the injury phase of CLE.[9]

Increased number of skin homing cytotoxic T lymphocytes associated with expression of IFN-α inducible protein MXA results in scarring skin lesions of DLE.[45]

B Cells

The production by B cells of auto antibodies against nuclear antigens is the hallmark of SLE.[46]

These auto antibodies form immune complexes and induce tissue damage in LE.[9]

B cells may not be important in CLE which is supported by the suggestion that anti B cell therapies (Rituximab) are less effective for CLE.[9]

Clinical Features

The classical DLE lesion begins as red purple macules, papules or small plaques and subsequently develops a hyperkeratotic surface. Early classic DLE lesions typically evolve in to well defined, sharply demarcated erythematous discoid plaques covered by an adherent scale that extends in to the orifices of dilated hair follicles.[9]

Discoid plaques vary in size from a few millimeters to 10 – 15cm.[11]

When the adherent scales are removed, the undersurface shows horny plugs that have occupied dilated pilosebaceous canals. This is called carpet tack (or) tin tack sign (or) cat's tongue sign.[47] The carpet

tack sign is also seen in localized pemphigus foliaceus[48] and in seborrhoeic dermatitis. DLE lesions typically expand with erythema and hyper pigmentation at the periphery.[9] Lesions spread centrifugally and merge. Resolution of lesions results in atrophy and scarring with pigmentary changes. In Asian Indians the disease may present as macular hyper pigmentation.[9]

Wide follicular pits containing blackheads or scale occur mainly in the concha or triangular fossa of the ear termed Shuster's sign; occur in up to 1/3rd of cases of DLE.[49] But they also occur in SLE.

Localized cribriform scarring occurs mostly on the face.[11]

Localized DLE (LDLE)

Localized DLE indicates only the head and neck involvement affected.[50] Face is most commonly affected.[51] Scalp, ears, nose, arms, legs and trunk are affected to a lesser extent.[11]

The lesions may be bilateral (not necessarily be symmetrical) or unilateral.[11]

Disseminated DLE (DDLE)

Characteristic lesions of DLE that occur in a widespread pattern on the trunk and limbs are termed as disseminated (or) widespread DLE.[11]

The appearance may be indistinguishable from the papulo-squamous type of SCLE, but scarring occurs in most patients,[11] in contrast to SCLE lesions that are non-scarring.[52] Distribution of lesions may occur in a wide spread pattern on the trunk and limbs.[11] Lesions on the dorsa of the hands, palms or toes occurred in 6% of patients.[11]

Disseminated lesion with reticulate telangiectasia was described. This type of telangiectasia is possibly similar to 'lupus erythematosus telangiectoides', first described by Crocker. [53]

Other variants encountered in disseminated DLE are annular, bullous [54], linear (following Blaschko's lines) [55] and arteritic lesions have been reported.[11] Annular variant of DDLE has been called lupus erythematosus gyratus repens.[11]

Variants of Discoid Lupus Erythematosus

Hypertrophic (or) Verrucous DLE, Lupus panniculitis with DLE, Tumid LE, Chilblain lupus, Mucosal DLE, Lichenoid DLE (LE / LP overlap, lupus planus)[9] were the variants of DLE.

Hypertrophic (or) Verrucous DLE

Hypertrophic DLE was first described by Behcet as Lupus erythematosus hypertrophicus et profundus in 1940.[56] [57] Verrucous

lesions with raised, indurated edges are most frequently reported on extensor aspect of the forearms, face and upper trunk.[58] Other sites where warty lesions are most commonly seen are nose, temples, ears and scalp. Difficulty in walking is associated with lesions on palms and soles.[11]

Hyperkeratotic papulonodular lesions resembling keratoacanthoma, hypertrophic lichen planus[59] or nodular prurigo also occurs in verrucous DLE. Usually hypertrophic DLE patients have classic DLE lesions elsewhere in the body.[60]

The lesions are characterized by dull, red indurated unique or multiple papulonodular lesions covered with keratotic scale or as larger plaques covered by an adherent multilayered ostraceous horny white or yellowish material or as regionally diffuse hyperkeratosis that resemble as chalky dust applied over the skin.[61] Hypertrophic DLE rarely develops to systemic lupus erythematosus.

Lupus Panniculitis

Lupus panniculitis has been referred as Kaposi – Irgang disease (or) Lupus erythematosus profundus.[9] It can occur at any age and has been reported in childhood.[62] They are firm, rubbery, sharply defined, persistent nodular lesions of varying sizes.[11] Classical lesions of DLE

may be found elsewhere. The lesions of lupus panniculitis heal with depressed areas or anetoderma.[11] Dystrophic calcification and ulcerations occur in older lesions.[9] [61]

Breast nodules in LE panniculitis has been called lupus mastitis and may herald SLE. [63] Most lesions are usually found in areas of increased fat deposition such as the trunk, buttocks, proximal upper and lower extremities, but the shoulders and thighs are further sites of predominant involvement. [61] Lesions may also develop on scalp, parotid region and periorbital tissues. [61] [64] [65]

LEP can be found in approximately 2-10% of patients with SLE.[61] Roughly 50 percent of patients with LE profundus/panniculitis have evidence of SLE. [11]

Some have used the term LE profundus to designate those patients who have both LE panniculitis and DLE lesions and LE panniculitis to refer to those having only subcutaneous involvement.[11]

Tumid Lupus Erythematosus (LET)

Tumid LE is a rare subtype of chronic cutaneous lupus erythematosus that was first described by Gougerot and Bournier in 1930.[66] LET is characterized clinically by erythematous, edematous, succulent, non scarring plaques in sun exposed regions. [67]

In a study of 40 patients of LET 70% of the patients showed a remarkable photo sensitivity and complete resolution of skin lesions with antimalarial therapy. [67] [68] In about 10% of the patients, ANA were detected. There was no evidence of underlying systemic involvement in any of the patients. [67] [68] Tumid lesions have tendency to recur.[68] The main differential diagnoses are polymorphic light eruption, Jessner's lymphocytic infiltration of the skin, reticular erythematosus mucinosis and pseudo lymphoma. [67]

Chilblain lupus Erythematosus / perniotic LE:

Chilblain LE is seen commonly in women [69] the lesions result from micro vascular injury secondary to cold exposure and due to hyper viscosity from immunological abnormalities.[69] Clinically the lesions develop on the toes, fingers and face as purple-red patches, papules and plaques. As they evolve, assume the appearance of scarred atrophic plaque with telangiectasia.[9] Ulceration is common in digital pulp lesions and sole lesions go in for necrosis easily.[70] Anti–Ro/SS-A antibodies are the auto antibodies encountered in chilblain lesions.[71] Persistence of lesions beyond the cold months, a positive ANA or presence of one of the ACR (American college of rheumatology) criteria for SLE helps to distinguish chilblain LE from idiopathic chilblains.[72]

Nearly twenty percent of patients with chilblain LE later develop SLE.[9]

Mucosal DLE

Oral mucosa is most frequently affected.[9]

The prevalence of mucous membrane involvement in chronic cutaneous LE is about 25%.[9] Nasal, conjunctival and genital mucosal surfaces can also be affected.[73]

With in the mouth, buccal mucosa is most commonly involved. Individual lesions begin as painless, erythematosus patches later mature in to chronic plaque having a sharply marginated irregularly scalloped white border with radiating white striae and telangiectasia in buccal mucosa.[9] Plaques on palatal mucosa show hyperkeratotic white strands with encircling zones of punctate erythema giving a honeycomb appearance.[73] Older lesions develop central depression and painful ulceration.[73]

Chronic DLE plaques appear on the vermillion border of the lips, involvement of the lips present as a diffuse cheilitis especially on the more sun exposed lower lip.[9]

Chronic mucosal DLE lesions can develop malignancy like squamous cell carcinoma.[73] The prevalence of mucosal involvement in LE patients is debatable. Some authors suggest that the prevalence of oral lesion in SLE is about 9–45% where as it is about 3–20% in patients with Cutaneous lupus erythematosus. [74, 75, 76, 77]

LE/LP Overlap syndrome:

Hypopigmented atrophic patches and plaques with livid red to bluish violet color showing telangiectasia and scaling on the surface[154] is the clinical picture. These lesions are usually seen in the extremities.

Classic lesions of both LP and discoid lupus erythematosus (DLE) are uncommon in LE/LP overlap but the morphology share features of both the disease.[78]

Histopathology reveals a lichenoid infiltrate characteristic of LP and LE features in the same biopsy.[80]

Direct immunofluorescence (DIF) aids in diagnosis in histologically doubtful cases, revealing colloid bodies staining with IgG, IgM and C3 in the epidermis or at the dermoepidermal junction (DEJ) as seen in classic LP.[81] Linear to granular deposits of IgM and C3 suggesting LE are also visible in DIF rarely.

Drugs found effective in this syndrome are oral retinoids, ciclosporin [82] and hydroxychloroquine [83]

Progression of LE/LP syndrome to SLE is 5-10% [79]

Nail changes in DLE

Subungual hyperkeratosis is more common than the red-blue discoloration of the nail plate with longitudinal striae and crumbling away of the nail. [84]

Eye lesions in DLE

Lesions are more common on the lower eyelid, outer one third. Palpebral lesions without lesion elsewhere on the face have been reported. [85]

The different ocular manifestations and complications of DLE [86-94] were

Orbit - Proptosis, Periorbital edema

Eyelids - Chronic blepharitis, lashloss, scarring, destruction and disfigurement, ectropion, entropion, trichiasis, panniculitis, pigmentary changes

Conjunctiva - Conjunctivitis, hypertrophic / verrucous lesion, scarring symblepharon

Cornea - Stromal keratitis

Acute mucinosis of the eyelids and periorbital skin can occur. [95]

Scarring Alopecia in DLE:

The lymphocytic infiltrate in perifollicular region was more around the mid-follicle at the level of the sebaceous gland. [96] The changes observed were alteration in the expression of the matrix molecules, the proteoglycans in the connective tissue sheath and in the keratin intermediate filaments of the outer root sheath cells at the mid follicular level in normal and diseased scalp [96]. Loss of stem cells in the bulge region plays a major role resulting in cicatricial alopecia in DLE lesions. [96] There was a marked reduction in sebaceous glands size in the diseased scalp. [96] 34% of DLE patients expressed features of scarring alopecia [96] in a study by Wilson et al. 41.9% of all scarring alopecia were due to DLE. [97]

Associated conditions

Small telangiectasia on face, dilated nail fold capillaries, mild diffuse alopecia, alopecia areata,[98] bilateral parotid enlargement,[99] livedo reticularis on legs,[100] Porphyria (cutanea tarda, variegate, acute intermittent, erythropoietic protoporphyria) Pemphigus, Myasthenia

gravis, Thymoma, Chronic lymphocytic leukaemia, Macroglobulinaemia, Benign monoclonal gammopathy, Multiple myeloma, Polychondritis, Thyroiditis,[101] Carpal tunnel syndrome, Polymorphic light eruption[102,103,104] Sheehan's syndrome, vitiligo,[105] systemic sclerosis (scleroderma) [106] have been reported in association with DLE.

Histopathology of Discoid Lupus Erythematosus

Discoid lesions show changes that may be apparent at all levels of the skin, but all need not be present in every case. [107]

Stratum Corneum:

Hyperkeratosis with keratotic plugs found mainly in dilated follicular openings and in openings of eccrine ducts as well. [107]

Epithelium:

The epithelium shows thinning and flattening of stratum malphighii and these changes vary with the clinical character of lesions. [107]

Hydropic degeneration of basal layer is the most significant histological change. [107]

Basal keratinocytes show individual cell necrosis and squamatization. [107]

Basement Membrane:

The basement membrane appears thickened and tortuous in long standing lesions correlating with deposition of immunoreactants. [107]

With PAS stain, Basement membrane thickening becomes more apparent at dermal– epidermal interface, follicular – dermal junction [107] and in capillary walls.

Stroma:

The stroma shows a predominantly lymphocytic infiltrate admixed with plasma cells along the dermal-epidermal junction, around hair follicles and sebaceous glands. [107] The impinging infiltrate on pilosebaceous units leads to gradual atrophy and its disappearance. [107]

Patchy lymphocytic infiltrate in an interstitial pattern and around eccrine coils with extension into subcutaneous fat [107] may be present. Interstitial mucin deposition, dermal edema, vasodilatation and extravasations of erythrocytes, pigmentary incontinence and colloid bodies are seen in DLE lesions. [107]

Mucin deposition (hyaluronic acid) is common in mid and lower dermis and is best demonstrated with colloidal iron (or) Alcian blue stains. [108]

Verrucous Lupus Erythematosus

Verrucous LE show two patterns histologically:

1. Epidermal hyperplasia with papillomatosis and surmounted by hyperkeratotic scale. Dyskeratotic keratinocytes with band like mononuclear cell infiltrate along the dermal – epidermal junction. [107]

2. Cup – shaped keratin filled crater surrounded by an acanthotic epidermis with elongated rete ridges and a sparse mononuclear infiltrate [107] with dermal changes similar to DLE.

Lupus Erythematosus Profundus / Panniculitis

LE Panniculitis is a mixed type of panniculitis [109] that reveal a deep lymphocytic infiltration in the fat lobules and in the septa. [110,111]

Lymphoid aggregates (or) germinal (or) follicular centers are commonly seen. [110,111,109]

Hyaline necrosis of fat is the distinctive feature where the fat cells having lost their nuclei show deposit of fibrin and other proteins in an eosinophilic matrix between residual fat cells. [110,111]

Calcification is a feature seen in older lesions. [111]

Lymphocytic infiltration of blood vessels is also seen in LE panniculitis.

Tumid lupus Erythematosus

Superficial and deep dermal perivascular, interstitial and periappendageal lymphocytic infiltrates with stromal mucin deposits. Epidermal changes are not observed in this type. [9,107] Focal interface changes at dermoepidermal junction and at follicular infundibula are observed in few studies. [112]

ANA in Discoid Lupus Erythematosus

In the strict sense, antinuclear antibodies are auto antibodies directed against nuclear specificities, such as DNA or small nuclear ribonucleoproteins (snRNPs). [113]

With the advent of the fluorescent antinuclear antibody test (FANA), auto antigens through out the cell can be detected. Thus ANAs

has expanded to include a diverse spectrum of nuclear and cytoplasmic specificities. [113]

Thus ANAs have established collaboration between clinical immunology and molecular biology. [113]

The evolution of the ANA technique range from the subjective (LE cell preparation) to immunofluorescence ANA (ANA – IFA) performed in a variety of substrates to the automated objective (ANA – EIA). [114]

The major development in ANA screening tests was the development of the indirect ANA – IFA in the 1950s. [114]

Thus the evolution from subjective to objective method, from manual to automated procedures provided the benefits like lowered costs for ANA tests and the potential for improving the consistency of performance of the ANA test by objective data. [114]

Fluorescent anti nuclear antibody (FANA):

FANA provides a rapid, yet highly sensitive screening method for ANA detection. Test sera at varying dilutions (typically serially increasing by twofold) are incubated with substrate cells, and bound antibodies are detected by fluorescein-conjugated anti–human IgG, followed by visualization via a fluorescence microscope. [115] Results

typically are reported by two parameters—pattern and titer—with any pattern of reactivity at a titer of 1:40 or greater being considered positive. [115]

Enzyme Linked Immuno-Sorbent Assay (ELISA):

ELISA provides highly sensitive and rapid technique for the detection of ANAs and determination of antibody specificity. [116] Test sera are incubated in wells precoated with purified target antigen; bound antibodies are detected via an enzyme conjugated anti-human immunoglobulin antibody, followed by color visualization with the appropriate enzyme substrate.[116] This technique can denature auto antigens and can produce some false positive results which require further confirmation. Because of their ease of use, ELISAs continue to play a prominent clinical role. [116]

Target auto antigen and their ANA pattern in SLE: [116]

Target auto antigens	**ANA Patterns**
dsDNA, ssDNA	Rim, Homogenous
Nucleosome structure	Homogenous, Rim
H1, H2A / B, H3, H4	Homogenous, Rim
H3	Large speckles
CENP-A, -B ,-C, -D	Speckles

Target auto antigens	ANA Patterns
PCNA	Nuclear / nucleolar speckles
Sm core B'/B, D, E, F, G	Speckled
U1snRNP70K, A, C, U2snRNP, U5snRNP, U7snRNP, SR	Speckled
Ro ,La	Speckled
RNAPII	Nuclear / nucleolar
Ribosomal RNPs	Nucleolar, cytoplasmic

ANA positivity in DLE patients ranged from 2.7% to 68.5% in various studies. [117,118,119,120]

ANA were commoner in older patients, in those who had suffered from the disease for longer periods or had more extensive skin involvement. [121] Regarding the pattern of ANA, the 'homogeneous' type of antinuclear factor was reported twice as frequent as the 'speckled' type in LE.

Anti DNA antibodies- incidence varies from 0-27% [122,123,124] IgM antibodies to single strand DNA occur in one-fifth of patients and may indicate widespread, progressive disorder [123]

Anti Ro antibodies in low titre are found in 10% of DLE [11]

Direct immunofluorescence:

Direct immunofluorescence has a significant value in the evaluation of patients with active cutaneous connective tissue disease. The intensity of the deposits of immunoreactants along the basement membrane in these patients correlates with the degree of interface/lichenoid dermatitis/ mucositis. [125]

In discoid lupus erythematosus, the most common immunoreactants visualized with direct immunofluorescence is IgM. [125]

Procedure

A 4mm punch biopsy is taken from the lesion and non sun exposed uninvolved skin. For optimal results, an established lesion (present for 3 months or longer) that has not been treated is submitted for study the specimen is washed with normal saline and sent in normal saline with in 24 hrs.

While processing, the specimen is washed several times in phosphate-buffered saline, snap frozen, sectioned, and incubated with fluorescein-conjugated antisera to IgA, IgM, IgG, and the third component of complement (C3) and then visualized under fluorescent microscope.

In a positive test, there is continuous granular deposition of usually two or more immunoreactants (in a band) along the dermal-epidermal junction [107] .Variables that affect DIF results are the site of the biopsy (sun-exposed vs. sun-protected), duration of the lesion (acute, sub acute, chronic), disease activity and preceding therapy [107] .Lesions on the head, neck, and arms are positive more frequently (80 percent) than those on the trunk (20 percent) [9]

DIF in DLE shows deposition of immunoreactants in specimen from sun exposed untreated lesions. The positivity in DLE lesion is more than 90% in untreated lesion and almost negativity in sun exposed uninvolved region. No deposition of immunoreactants in nonsunexposed uninvolved region in DLE.

DIF in SLE shows deposition of immunoreactants in untreated lesion of sun exposed region, sun exposed uninvolved region and in nonsun exposed uninvolved region. The positivity is about 80 to 90% in untreated lesion, more than 80% in sun exposed uninvolved skin, more than 91% in nonsunexposed uninvolved skin in active SLE and 33% in nonsunexposed uninvolved skin in inactive SLE, this indicates renal involvement. Thus DIF in LE varies depending on the prior treatment, disease activity and the site of biopsy.

The lupus band test, described as positive when granular IgG is present along the basement membrane zone in specimens from sun-protected nonlesional areas and has been abandoned due to its unreliability and current availability of the other more reliable methods for early diagnosis and prediction of systemic disease in lupus erythematosus. [126]

LE Profundus:

Immunoglobulin and complement deposits are usually found in blood vessel walls of the deep dermis and sub cutis [9]. Immunoglobulin deposits at the dermal-epidermal junction may or may not be present, depending on the site of biopsy, the presence or absence of accompanying SLE, and the presence or absence of overlying changes of DLE at the dermal-epidermal junction. [9]

ARA criteria for SLE:

According to revised ARA criteria 4 or more criteria out of 11 should be present serially or simultaneously to establish the diagnosis of SLE.

The muco cutaneous criteria included are photosensitivity, malar rash, discoid rash and painless oral or nasopharyngeal ulcers [9]

The systemic features in the criteria are rheumatologic manifestation in the form of arthritis, serositis, renal manifestation including persistent proteinuria or cellular casts, neurological features in the form of seizures or psychosis in the absence of underlying medication or metabolic derangements and hematological dysfunction including hemolytic anemia or leucopenia or lymphopaenia or thrombocytopenia [9].

The immunological criteria include two features viz. the presence of high titre of anti-nuclear antibody and antibodies to naïve DNA or antibody to Sm nuclear antigen or antiphospholipid antibodies in the form of anti cardiolipin antibody, lupus anticoagulant or false positive serological test for syphilis persisting for more than 6 months. [9]

The Systemic Lupus International Collaborating Clinics (SLICC) group proposed revision and validation of the ARA criteria for SLE in 2012. [131]

The SLICC classification system includes 11 clinical criteria and 6 immunological criteria. [131] The additional validation in this criteria aside ARA criteria are inclusion of all types of LE-specific lesion and its variants and have included non-scarring alopecia as a separate criteria. [131] Importance is given for urine protein-creatinine value in renal pathology. Under neurological manifestation apart from seizures and

psychosis they have included acute confusional state, mononeuritis multiplex, myelitis and peripheral or cranial neuropathy. [131]

Low complement and direct coomb's test are included additionally in immunologic criteria in the SLICC classification system. [131]

Four criteria of which a minimum of one clinical and one immunological criterion should be present or features of lupus nephritis in renal biopsy with ANA or antids - DNA should be there to establish the diagnosis of SLE [131]

The validated SLICC classification criteria are more consistent with emerging concepts of SLE pathogenesis when compared to revised ARA criteria. [131]

Neoplasm in DLE:

Squamous cell and less frequently, basal cell carcinomas occur in the scars of DLE, particularly on the scalp, ears, lips and nose [127] keratoacanthoma [128], malignant fibrous histiocytoma [129] and atypical fibroxanthoma [130] in DLE lesions have been reported.

Squamous cell carcinoma arising in discoid lupus erythematosus lesion is rare; there are reports of SCC occurring on DLE lesions over scalp and upper lip. [134]

Most cases of SCC have been reported in sun-exposed region in whites. A case of squamous cell carcinoma arising in DLE scars in sun-protected region has been reported. [132]

Numerous squamous cell carcinomas in the scars resulting from discoid lupus [133] are also reported.

Course of DLE and its association with SLE:

Approximately 5 percent of patients presenting with isolated localized DLE subsequently develop SLE [9]. The progression risk is more in patients with disseminated DLE (22%). [11] Well-defined discoid lesions with atrophic scarring, as seen in DLE, occur in about 15% of SLE patients [107]. These DLE lesions may precede all other clinical features of SLE. Most of the SLE patients with preceding DLE will have a relatively benign course [119]

Risk factors for the progression of SLE in DLE patients:

The presence of SCLE / ACLE skin lesions; diffuse non-scarring alopecia, LE-non-specific skin lesions such as vasculitis, periungual nail fold telangiectasia, Raynaud phenomenon; generalized lymphadenopathy clinically and unexplained anemia; marked leucopenia; false-positive tests for syphilis; hypergamma-globulinemia; an elevated erythrocyte

sedimentation rate (especially > 50 mm/hour); persistently positive high-titer ANA assay; anti-single stranded DNA antibody; positive, sun-protected, non-lesional lupus band test (LBT) and high levels of soluble IL-2 receptor[9] on investigation were the risk factors for progression to SLE.

AIM OF THE STUDY

1. To find out the clinical profile of discoid lupus erythematosus seen among patients attending the skin OPD.

2. To find out the other dermatological and systemic associations in discoid lupus erythematosus patients.

3. To study and correlate the various clinical parameters with both types of discoid lupus erythematosus and its morphological variants.

MATERIALS AND METHODS

The material for this study was from the patients attending the skin OPD, Government Rajaji Hospital, Madurai Medial College, Madurai during the period from October 2010 to September 2012.

Inclusion criteria

1. Patients clinically diagnosed to have discoid lupus erythematosus lesion and confirmed by histopathological examination.

2. Clinically doubtful cases but confirmed by histology were included.

Exclusion criteria

1. Patients who did not give consent for biopsy were not subjected to biopsy procedure and were excluded.

2. Patients who did not have clinico-pathological correlation were also excluded.

A total of 51 patients clinically diagnosed to have discoid lupus erythematosus during this period were taken for the study. A detailed clinical history including the age at onset, duration, triggering factors, systemic symptoms, and family history were elicited. A complete general

examination, systemic examination, dermatological examinations were made. Digital photographs were taken.

The type, morphology and distribution of the skin lesions, the presence of other cutaneous and systemic associations were noted. Laboratory investigations included complete blood count, urinalysis, renal function test, erythrocyte sedimentation test (ESR) was done. Antinuclear antibodies (ANA) were detected using Hep-2 cells as substrate by immunofluorescence technique or by ELISA method in 30 patients.

Skin biopsy was done in all the patients after obtaining informed consent. After cleansing the area of the lesion chosen for biopsy with spirit, 2% lignocaine was infiltrated in to the area and tissue specimen was obtained by punch biopsy technique. The specimen were preserved in 10% formalin and submitted for histopathological examination to the department of Pathology, Madurai Medical College.

Direct immuno fluorescence was done only for 5 patients due to financial constraints and patients were already on partial treatment during examination. The biopsies were taken from the lesion and also from non sun exposed uninvolved skin and preserved in normal saline and sent to the private laboratory for immunofluorescent study on the same day.

OBSERVATIONS AND RESULTS

A total of 51 patients with discoid lupus erythematosus who attended the out patient department in the department of Dermatology, Government Rajaji hospital, Madurai medical college, from October 2010 to September 2012 were included in the study. Incidence in this study was 0.47 per 1000 cases among patients attending Dermatology clinic. The following observations were made.

Table1: Clinical type of DLE

Clinical type of DLE	No. of patients	Percentage (%)
Localized	30	58.82
Disseminated	21	41.17

The localized type was found to be more common than disseminated type.

Table 2: The age of onset

Age of onset	Localized	Disseminated	Total	Percentage %
0-10	-	-	-	-
11-20	-	2	2	3.9
21-30	6	5	11	21.56
31-40	11	8	19	37.25
41-50	6	6	12	23.52
51-60	5	-	5	9.8
61-70	2	-	2	3.9

The majority of the patients (58%) had disease onset between 21-40years of age. 1 female patient with disseminated lesions had onset of the disease during her pregnancy.

Table 3: Sex distribution

Type of DLE	Male	Female
Localized	3	27
Disseminated	7	14

Female to male ratio - 4.1: 1

The female to male ratio in localized type is 9:1 and in disseminated type it is 2:1. Localized type was observed more common among female patients. Among male patients disseminated type was seen in higher proportion (7 of 10 i.e.70%)

Table 4: Duration of the lesion

Duration	Localized	Disseminated	Total	Percentage
<1 year	14	7	21	41.17
1-5 years	12	6	18	35.29
5-10 years	2	3	5	9.8
10-15 years	2	3	5	9.8
15-20 years		2	2	3.9

About 76% of patients had lesions less than 5 years of duration. 19% of cases had disease for about five to fifteen years. Lesions beyond 20 years were found in 2 patients (3.9%) with disseminated lesions. One among the 2 satisfied ARA criteria.

Table 5: Triggering factors

Inducing or trigger factor	No. of patients	Percentage %
Occupation-(excessive UV exposure)	25	49.01
Drugs	11	21.56
Viral infection	2	3.9
Trauma /burns	4	7.84
Smoking	8	15.68

Occupation related to excessive sun exposure was found in 25 patients (49%). Prior history of drug intake was present in 11 patients (21%) such as anti tuberculosis drugs-isoniazid, anti hypertensive drugs, thyroxine and anti psychiatry drugs. History of preceding viral infection was elicited in 2 (3.9%) patients. Out of the total 10 male patients, 8 of them (15% of study group) i.e. 80 % were smokers.

Table 6: Variants of DLE

Variants	Localized	Disseminated	Total	%
Classical	16	5	21	41.17
Classical,Mucosal	11	11	22	43.13
Classical,Mucosal,verrucous	-	2	2	3.9
Classical,Mucosal,tumid	1	-	1	1.9
Classical,Verrucous	-	1	1	1.9
Classical,Panniculitis	-	1	1	1.9
Verrucous	1	-	1	1.9
Tumid	1	-	1	1.9
Panniculitis	-	1	1	1.9

Table 7: Variants of DLE

Variant	No.of patients	Percentage
Classical	48	94%
Mucosal	25	49%
Verrucous	4	7.8%
Panniculitis	2	3.9%
Tumid	2	3.9%

Among the variants, classical DLE was seen in 94% of study group of which 28 patients were of localized type and 20 patients were of disseminated type. Mucosal manifestation was found in 25 patients (49%). Verrucous or hypertrophic DLE was seen in (7.8%) 3 male patients and in one female. Lupus panniculitis and tumid lesions were seen in 2 patients (3.9%) each respectively

Distribution of lesion:

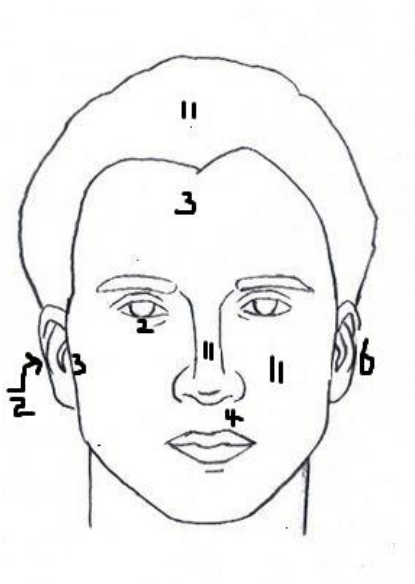
Table 8 - HEAD and NECK involvement

Site	Localized	Disseminated	Total	%
Scalp	11	15	26	50.98
Forehead	3	10	13	25.49
Eyelid	2	-	2	3.9
Nose	11	4	15	29.41
Cheek	11	9	20	39.21
Ear	6	12	18	35.29
Preauricular	3	-	3	5.8
Perioral	4	-	4	7.8
Postauricular	2	1	3	5.8
Neck	-	3	3	5.8

The central region of the face namely the nose, cheek region, eyelid, perioral involvement is more commonly involved in localized type.

Scalp involvement was observed in 50% cases. Thirty nine patients had lesions on face constituting 76%. In face cheek was found to be the common site seen in 39% of study group. Concha sign was seen in 35% of patients.

Localized DLE- involvement of head & neck



DisseminatedDLE- involvement of head & neck

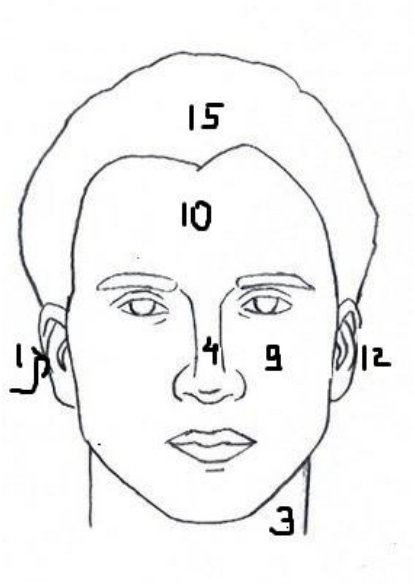


Table 9 – Involvement of sites other than head and neck

Site	Localized	Disseminated	Total	%
Upper limb	-	19	19	37.25
Trunk	4	19	23	45.09
Lower limb	1	7	8	15.68

Four patients (7.9%) with single to few lesions restricted to involvement of one region alone namely chest, lower back, gluteal region without head and neck lesions are included in the localized type in our study. One patient with only 2 lesions, on concha and the other one on chest was also categorized as localized type.

Widespread involvement is more commonly noticed in disseminated type. The upper limb involvement was seen in 37%, trunk involvement in 45% and lower limb was involved in 15% of study group. The lesions on lower limb are encountered only in 7 patients with disseminated lesions.

Table 10: Distribution of lesion in relation to sun exposure

Type	Sun exposed site	Exposed and unexposed sites	Un exposed site
Localized	29	-	1
Disseminated	21	13	13

One elderly female had localized verrucous DLE only on both gluteal regions.

Unexposed /covered site involvement seen in [14/51]-27.4% of total DLE patients

Unexposed /covered site involvement seen in disseminated DLE-[13/21] -61.9%

Table 11: Total No of lesions

Type	<5	5-9	>10
Localized	20	10	-
Disseminated	2	4	15

Localized disease was classified as mild (<5), moderate (5-9) and severe (>10) depending on the total no. of lesions

Twenty among thirty patients (66%) had mild localized disease and 10 patients (33%) had moderate form of localized disease. None of the patient had severe form of localized disease.

Table 12: Mucosal pattern of involvement

Morphology	Upper lip	Lower lip	Buccal mucosa	Palate	Gingiva
Discoid	10	20	-	-	-
Erythematous plaque	-		1	-	-
Depigmented / white patches	-	-	2	1	2
Ulcerated plaque / cheilitis	-	1	-	-	-
Erosion	-	-	-	2	-
Total	**10**	**21**	**3**	**3**	**2**

Classical discoid lesions are the most common mucosal pattern. 49% of the study group had mucosal lesion.

Table No 13: Site of mucosal involvement

Mucosal site	**No. of patients**	**Percentage %**
Upper lip	10	40
Lower lip	21	84
Buccal mucosa	3	12
Palate	3	12
Gingiva	2	8

Lower lip was the commonest site involved in oral mucosa in our study observed in about 84% (21 of 25). The next common site being upper lip involved in 40%. Nine patients (36%) had involvement of both upper and lower lip.

Table No 14: Pattern of mucosal involvement

Pattern	**No. of patients**	**Percentage %**
Discoid	21	84
Erythematous plaque	1	4
Depigmented / white patches	2	8
Ulcerated plaque / cheilitis	1	4
Erosion	2	8

The discoid lesion was observed in 84% of patients with mucosal involvement. Depigmented white patches were seen in 2 patients (8%). Cheilitis and erythematous plaque were observed in 1 patient each i.e.4%. Palatal erosion was seen in 2 patients (8%).

Table 15: Alopecia in DLE

Type	Scalp lesion	Disfiguring Scarring alopecia	Diffuse nonscarring alopecia
Localized	11	10	-
Disseminated	15	10	3

Twenty six patients had scalp lesions constituting 50% of study group. Twenty out of twenty six patients (76%) had disfiguring scarring alopecia. Six patients (23%) only had few small lesions over scalp with out much disfiguring scarring alopecia. Three patients with disseminated DLE had diffuse non scarring alopecia.

The Systemic Lupus International Collaborating Clinics (SLICC) group revised and validated the American College of Rheumatology (ACR) systemic lupus erythematosus (SLE) classification criteria in which they have included non scarring alopecia as one of the clinical criteria. Though all 3 patients with diffuse non scarring alopecia has not satisfied ARA criteria during the study period, follow-up is required and advised in all of them.

Anti Nuclear antibodies:

ANA was done in 30 patients, by FANA method in 15 patients and in another 15 by ELISA method. 7 among localized type and 15 among disseminated type showed ANA positivity. The granular/speckled pattern is the most common pattern observed by FANA method in our study. 73% (22/30) showed ANA positivity.

Table 16: ANA in DLE

ANA	Positive Localized	Positive Disseminated	Negative Localized	Negative Disseminated
ELISA	3	6	6	0
IFA	4	9	1	1

Table 17: Pattern in ANA by IFA

Pattern –ANA(IFA)	No of patients	
	Localized	Disseminated
Granular /Speckled	3	5
Homogenous	-	3
Nucleolar	1	-
Nuclear dots	-	1

Table 18: Histopathological findings

Histopathological findings	No. of Patients
Hyperkeratosis	47
Follicular plugging	46
Epidermal thinning	46
Basal layer degeneration (focal to diffuse)	51
Pigment incontinence	25
Subepidermal bulla	3
Inflammatory infiltrate Lymphocytic in upper dermis	48
Periappendageal	49
Perivascular	46
Interstitial	33
Pilosebaceous atrophy	15
Mucin deposition	5
Mixed Panniculitis	2
Carcinomatous changes- Horn pearls & individual cell keratinization	2

HPE showed classical features of DLE in all cases. Tumid lesions showed focal basal layer degeneration, perivascular, periappendageal inflammatory infiltrate with no epidermal changes. Mucosal lesion

showed features of basal layer degeneration with inflammatory infiltrate in the upper dermis and in perivascular region. 2 patients (3.9%) showed features of malignancy on clinico-pathological correlation.

Direct immunofluorescence:

Two cases with disseminated lesion showed deposits in both lesional and covered region. 1case of disseminated DLE showed no deposit both in lesional and covered region possibly due to treatment

Table 19: Direct immunofluorescence findings

Clinical picture	Deposits	Site	**1**.Lesional **2.**Nonsunexposed, Uninvolved	Comment
LEP	IgG,IgM, Fibrinogen	Septae of fat	1	LEP
LDLE	Ig G-band	BMZ	1	DLE
DDLE	IgG,IgA, fibrinogen	BMZ	1	LBT+
	IgG,IgA	BMZ	2	
DDLE	IgM,IgA,C3	BMZ	1	LBT+
	IgM	BMZ	2	
DDLE	No deposits	BMZ	1, 2	On treatment

LDLE—Localized DLE BMZ—Basement Membrane Zone

DDLE—Disseminated DLE LBT—Lupus Band Test LEP – LE panniculitis

Associations of DLE:

Twelve patients (23.5%) who satisfied ARA criteria had anti ds-DNA positivity. 13% (7/51) showed features of thyroid dysfunction in our study. One patient developed DLE lesions over herpes zoster site.

Table 20: Other LE features associated with DLE

Other LE features	No. of patients	Percentage %
Photosensitivity	42	82
Malar rash	2	3.9
SCLE	2	3.9
Oral ulcer	2	3.9
Arthralgia	20	39
Telangiectasia	1	1.9
Anaemia	8	15.6
Proteinuria	3	5.8
Lupus nephritis	1	1.9

Table 21: Cutaneous associations of DLE

Cutaneous associations	No.of patients	Percentage %
PLE	1	1.9
Melasma	2	3.9
Macular amyloid	1	1.9
Herpes zoster	2	3.9
Leprosy	2	3.9
Vitiligo	1	1.9

Table 22: Systemic associations of DLE

Systemic associations	No. of patients	Percentage %
SLE	12	23.5
Systemic sclerosis	1	1.9
Thyroid dysfunction	7	13.7

Complications:

1.Ulceration was observed in 2 patients on DLE lesions on lower limbs. Similarily ulceration was observed in LE panniculitis.

2. Squamous cell carcinoma over DLE lesion on arm and elbow respectively was observed in 2 patients with disseminated DLE.

DISCUSSION

Incidence:

In our study, the incidence of DLE was 0.47 per 1000 cases (51 among 106368 new cases) among patients attending the skin OPD during the period from October 2010 –September 2012. The incidence of DLE in one study was 3.56 per 100 000 persons. [8]

Age distribution:

The age of the patients ranged from 15 to 70 years. The mean age at onset of the disease is 38.56 when compared to 36 and 31.4 years in other studies [120] [136]. The majority of the patients (19 patients or 37.25%) fall in the age group from 31-40 years. 30 of 51 patients or 58.81% of patients in this study fall in the age group from 21-40 years as against 78% in the study done by Bajaj et al[136].

Sex distribution:

Female to male ratio in our study is 4.1:1. Several studies show female predominance ranging from 2:1 to 5:1[117,118,119,120] .The female to male ratio in localized type is 9:1 and in disseminated type it is 2:1. Localized type was observed more common among female patients. Among male patients disseminated type (7 of 10) was found in higher

proportion in our study. Equal ratio and male predominance was reported in few studies. [137,138]

Familial incidence:

Family history of SLE with ACLE rash was seen in a daughter of the male patient with DDLE. Familial discoid lupus erythematosus among siblings have been reported in the literature [144,145]. Family history of SLE has been reported among 2 DLE patients in a study [120].

Inducing Factors:

UV exposure, viral infection, drugs and smoking reported as inducing factors of lupus erythematosus in the literature was also observed in our patients were in concordance.[17,18,20,28,29,30]

CLINICAL FEATURES:

Types of DLE:

Localized DLE was found in 30 patients (58.82%), Disseminated DLE in 21 patients (41.17%) similar to the study by Insawang et al [120]

Localized type of DLE was the commonest type in our study (58.82%). Five patients among thirty (16%) presented with single to few

lesions on sites other than head and neck were classified as localized type in our study.

Total No. of lesions:

Localized disease was classified into mild (number of lesions less than 5), moderate (5-9 lesions) and severe (more than 10 lesions) by Bajaj et al[136] depending on the number of the lesions. 20(66%) patients had mild localized disease, 10 (33%) patients had moderate localized disease in our study.

Distribution of skin lesions:

Face (76%) was the most commonly involved site which is in concordance with other studies done by Callen et al, Insawang et al. [119,120] followed by scalp(50%). Ear involvement in the form of concha sign or Shuster's sign was seen in 35% in our study. Shuster's sign occurs in up to 1/3rd [33%] of cases of DLE [49].

Scalp involvement was seen in 50% in our study, it was 40% in the study by Sandipan et al. Forehead lesions were seen in 25% in our study where as it was 65% in the Sandipan et al study. Nasal lesions were seen in 76% in Sandipan et al study it was lower 29% in our study. Cheek involvement was seen in 39% in our study, it was higher 78% in

Sandipan et al study. Lesions on trunk were seen in 45% in our study it was 27% in Sandipan et al study. Arms and forearms involvement were observed in 37% in our study it was 19% in the study by Sandipan et al. Lower limb involvement was seen in 15% in our study which is similar 11% in the Sandipan et al study. Involvement of forehead, nose, cheek and concha were lower in our study when compared to Sandipan et al. study. The trunk and upper limb involvement were higher in our study when compared to Sandipan et al. study.

The most of the patients had lesions on sun exposed region [50/51]-98%. The Unexposed /covered site involvement was seen in [14/51]-27.4% of both localized and disseminated DLE patients. The Unexposed /covered site involvement seen in disseminated DLE was [13/21] -61.9%.

Eye changes:

Eyelid discoid lesion, blepharitis, conjunctivitis, proptosis, periorital edema that have been observed in our study have been reported in literature [85-94]

Palms and soles involvement:

Two male and 1 female with disseminated DLE had palmoplantar lesions constituting 5.8% in our study. Verrucous lesions and ulceration of DLE lesion over legs was observed in patients with palmoplantar involvement.

Thus palmoplantar involvement is quite rare ranging from 0.98% to 2.27% in other studies [139,140]

Variants:

Mucosal DLE:

The lower lip (84%) was the most common site involved in the oral mucosa, discoid lesion (84%) involving the exposed part of lip was the most common pattern of involvement in our study. The buccal mucosa, palate and vermilion of lips (more the lower than the upper lip) are referred as the commonest sites for lupus oral lesions. [74,146,147,148] Sandipan et al in their study reported oral mucosal involvement in 7.84% and lip lesions in 31% [140], in our study mucosal manifestation was observed in 49% of patients. Both upper and lower lips were involved in 9 patients of 25 with mucosal involvement (36%).

The other oral manifestations were erythematous plaque (involving lowerlip and buccalmucosa), depigmented patches/white squamous (involving buccal mucosa, palate and gingival), cheilitis and palatal erosion in our study. 2 patients (3.9%) with palatal erosion had features of SLE.

The clinical aspects of mucosal lesions described in LE patients in the study by Lourencxo et al. were erythemato-squamous plaque, erythemato-atrophic plaque, erythemato-ulcerative plaque, squamous-discoid, atrophic-discoid, cicatricial-discoid, ulcerative, keratotic, purpuric, bullous, white-squamous, atrophic, hyperchromic etc [74]

Mucosal involvement was seen in 12 patients of localized disease and 13 patients of disseminated disease.

Verrucous or hypertrophic DLE:

In our study 4 patients (7.8%) had verrucous DLE which is higher when compared to the study by Insawang et al. i.e. 1.5% [120]

Lupus Panniculitis:

Erythematous tender sharply demarcated plaque over the forehead extending to scalp, with few tender plaque and nodules over mandibular region, proximal arms was the presentation in 1 patient. Two patients

(3.9%) had LE panniculitis in our study which was lower when compared to the study by Bajaj et al (9.1%) [136]. But was higher when compared to Insawang et al study, they reported LE panniculitis in 2.3% [120]

Tumid LE:

Two patients (3.9%) presented with tumid lesions over face. Bajaj et al. in his study reported tumid lesions in 18.2% of patients [136], but only 3.9% showed tumid lesions in our study. Tumid LE was reported in 0.8% in the study by Insawang et al. [120]

The site involved in our patients with tumid LE namely the nose and malar region (sun exposed region) is in concordance with the other studies [67]

Alopecia in DLE:

The patients with scalp lesions were 26(50.9%). Disfiguring scarring alopecia was found in 20 patients (39.21%) in our study, nearly similar (34%) to a study done by Wilson et al. [141] Diffuse hair loss was observed in 3 patients. The Systemic Lupus International Collaborating Clinics (SLICC) group revised and validated the American College of Rheumatology (ACR) systemic lupus erythematosus (SLE) classification criteria in which they have included non scarring alopecia as one of the

clinical criteria. [131] All 3 patients with diffuse non scarring alopecia during the study period have not satisfied ARA criteria, hence follow-up is advised in all of them.

Associations:

Course of DLE and its association with SLE:

In our study 3 patients of localized disease (5.8%) and 9(17.6%) with disseminated disease satisfied ARA criteria for SLE. The specific anti ds-DNA was positive in all patients who satisfied ARA criteria. According to literature nearly 5 percent of patients with isolated localized DLE subsequently develop SLE [9] and the risk is higher in patients with disseminated DLE (22%) [11]. Renal and hematological abnormalities were commonly involved in our study. Immunological tests (ANA, DIF) were not done in all the patients and are the limitation in our study.

Photosensitivity was present in 42 patients (82.3%). Photosensitivity was reported less among DLE patients when compared to SCLE, ACLE [118]. Photosensitivity was seen in 14.6% to 87% in various other studies of DLE patients. [118,119]

Arthralgia was present in 20 patients (39.2%) in our study compared to 47% in the study by Bajaj et al [136].

Malar rash was observed in 2 patients (3.9%) where as it was 16.2% in the study by Insawang et al. [120] Psoriasiform SCLE rash was seen in a patient with SLE along with few discoid lesions. In our study 2 patients (3.9%) had SCLE lesion which was 2.3% in the study by Insawang et al [120]

Oral ulcer was seen in 2 patients (3.9%) in our study, it was 13% in Insawang et al study [120]. Proteinuria was present in 3 patients (5.8%), in the other study it was 11.5% [120]. Established lupus nephritis was observed in 1 among the patients with albuminuria. Facial telangiectasia was observed in 1 patient (1.9%).

Other systemic associations were systemic sclerosis, thyroid dysfunction (in the form of auto immune thyroiditis, hypothyroidism, hyperthyroidism and goiter). The association with systemic sclerosis, [106] thyroiditis[101] have been reported in literature. 13% showed thyroid dysfunction in our study.

Cutaneous associations observed were PLE [102,103,104] in 1 patient, Hansen's disease in 2 patients and one had deformity, melasma in 2 patients and macular amyloid on lower limbs in 1 patient with scalp DLE. Vitiligo was observed in 1 patient with disseminated DLE.

The association of DLE with PLE [102,103,104] vitiligo[105] and primary localized cutaneous amyloidosis in lupus erythematosus [142] have been previously reported in literature. The pathogenesis in LE and leprosy was attributed towards marked decrease of CR1/E (complement receptor in erythrocytes), which may result in an altered clearance of elevated immune complexes [143]

Other coexisted condition was herpes zoster in 2 patients (3.9%).

Histopathology:

The classical histopathological findings were seen in all the cases of DLE and its variants. The most significant histological finding basal layer degeneration focal to diffuse was observed in 100%. Hyperkeratosis (92%), follicular plugging (90%), epidermal thinning (90%), pigment incontinence (49%), upper dermal lymphocytic infiltrate (94%), periappendageal (96%) and perivascular infiltrate (90%), interstitial infiltrate (64%), pilosebaceous atrophy (29%) was observed. Sub epidermal bulla was observed in the biopsy of 3 patients (5.8%) particularly from specimen over scalp lesions. Mucin deposition in the dermis was less observed in H&E section, seen only in 5 patients (9.8%). Histological diagnosis concurred with clinical diagnosis in 100% in the study conducted by David-Bajar et al [150] which is similar in our study.

Features of squamous cell carcinoma were seen in the biopsy of verrucous growth seen on DLE lesion from 2 patients (3.9%).

Anti nuclear antibodies:

ANA was done by ELISA method in 15 patients and by IFA (indirect fluorescent antibody) method in 15 patients. 22 of 30 patients (73%) showed ANA positivity in our study, compared to 68.5% in Insawang et al study [120]

Of 15 patients, 13 showed positive reaction by IFA method. The speckled /granular pattern was the most common pattern in our study seen in 8 of 13 (61%), followed by homogenous pattern in 3 of 13(23%). Nucleolar and nuclear dots pattern were observed in each patient respectively. The homogenous pattern was reported twice frequent as speckled pattern in other studies in LE. The speckled pattern that was observed frequently in our study was similar to the study by Insawang et al [120].

Based on staining intensity scaling was given from 1+ to 4+. Strong reaction was indicated as 4+, weak reaction by 1+. The staining intensity of more than 1+ was observed in 5 patients. 3 among these 5 patients showed other features of SLE.

Direct immunofluorescence:

DIF was done for 5 patients. Among the 3 patients with disseminated disease, 2 showed positive lupus band test and no deposits was found in 1 patient(possibly due to prior treatment). In lupus panniculitis, the deposits of IgG, IgM, fibrinogen was seen in septae of fat. The deposits of immunoreactants were found in lesional skin in localized disease in 1 patient.

Other laboratory and clinical parameters:

Elevated ESR more than 50 mm/hr was observed in 6 patients (11.7%) which was lower (30.39%) when compared to the study done by Sandipan et al [140]. Lymphadenopathy was found in 2 patients (3.9%) with disseminated DLE.

Complications and sequlae:

Two patients (3.9%) with disseminated disease developed squamous cell carcinoma on lesions over exposed sites such as lower back, elbow and arm respectively. Malignant change was observed in 1 male and in 1 female. The duration of the DLE lesion in both patients was 4 and 13years respectively. Thus 3.9% of DLE patients in our study

showed malignant change. Squamous cell carcinoma was reported in 1 patient in the study done by Sandipan et al[140]

Ulceration over DLE lesion was observed in leg lesions and over panniculitis plaque totally in about 3 patients (5.8%).

Scarring was observed in 18 patients (35%), pigmentary alterations in 8 patients (15%) in our study.

Interesting observation:

One patient with disseminated DLE developed herpes zoster in thoracic segment. After resolution of zoster she developed DLE lesion over the healed scar. The histopathological findings showed features consistent with DLE. Similar observation has been reported as isomorphic phenomenon though there was confusion in labeling it as isomorphic or isotopic phenomenon [149,135]

SUMMARY

Incidence

DLE constituted 0.47 per 1000 of the total patients attending the skin OPD during the study period.

Age

The age of the patients ranged from 15 to 70 years. 58.81% of patients were between 21-40 years of age.

Sex:

Female to male ratio in our study was 4.1:1.

Familial involvement:

Family history of SLE was observed in an offspring of male patient with disseminated lesions.

Clinical features:

Localized type constitutes 58.82%, disseminated type constitutes 41.17%. The variants observed in our study were mucosal DLE, verrucous DLE, LE panniculitis and tumid LE. Classical discoid lesion was present in 94% cases. Mucosal involvement was seen in 49%.

Hypertrophic DLE lesion, LE panniculitis, tumid LE was found in 7.9%, 3.8% and 3.8% respectively. There was significant overlap in the morphological variants studied.

Face was the most common site involved 76% followed by the scalp in 50%. Concha sign was found in 35%.

The lower lip was the most common site involved in the mucosa with discoid lesion being the most common pattern.

Verrucous lesions were commonly observed in elbows and knees.

Tumid lesions were seen in the nose and malar region of the face.

Panniculitis involved the face and the extremities in both the cases.

Scarring alopecia was observed in 39.21%.

Ocular involvement was in the form of discoid lesion in the lower eyelid with blepharitis and conjunctivitis. Proptosis and periorbital edema was also observed.

Palmo plantar involvement was noticed in 5.8%.

Histopathology:

HPE findings were consistent with the diagnosis in all cases in whom biopsy was done. Focal to diffuse basal layer degeneration was seen in all the patients studied (100%).

ANA test:

23 of 30 patients showed positivity. The speckled/granular pattern was the most common pattern in IFA method in our study. The staining intensity of more than 1+ was observed in 5 patients.

Direct immunofluorescence:

DIF was done for 5 patients. 2 of them showed positive lupus band test.

Associations:

5.8% of localized disease and 17.6% with disseminated disease satisfied ARA criteria for SLE and showed antids-DNA positivity.

Other systemic associations were systemic sclerosis, thyroid dysfunction (in the form of thyroiditis, hypothyroidism, hyperthyroidism and goiter).

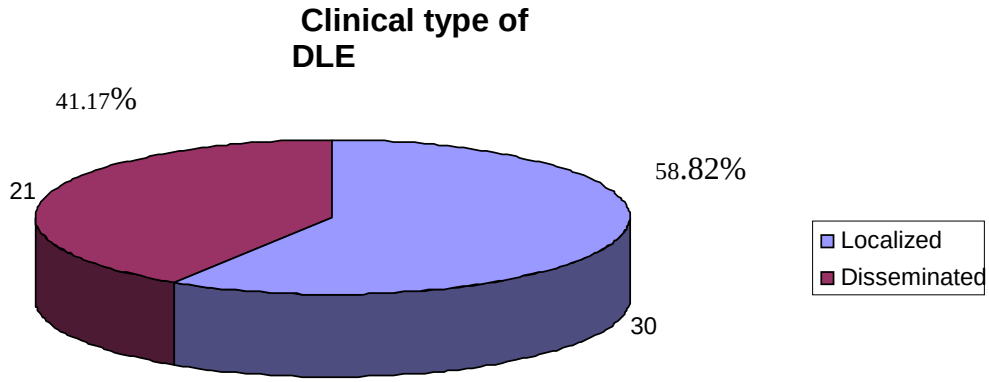
Cutaneous associations observed were PLE, Hansen's disease, melasma, macular amyloid and vitiligo.

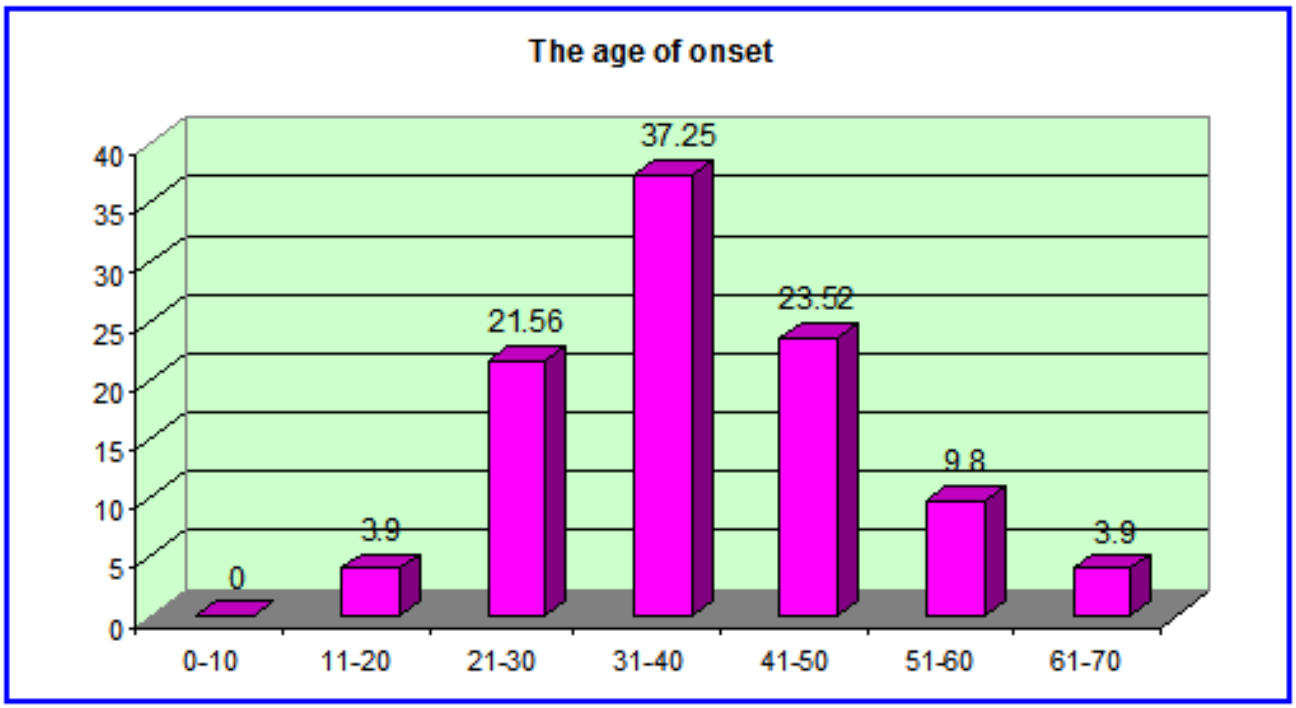
Neoplasm:

Two patients with disseminated disease developed squamous cell carcinoma on lesions over exposed sites.

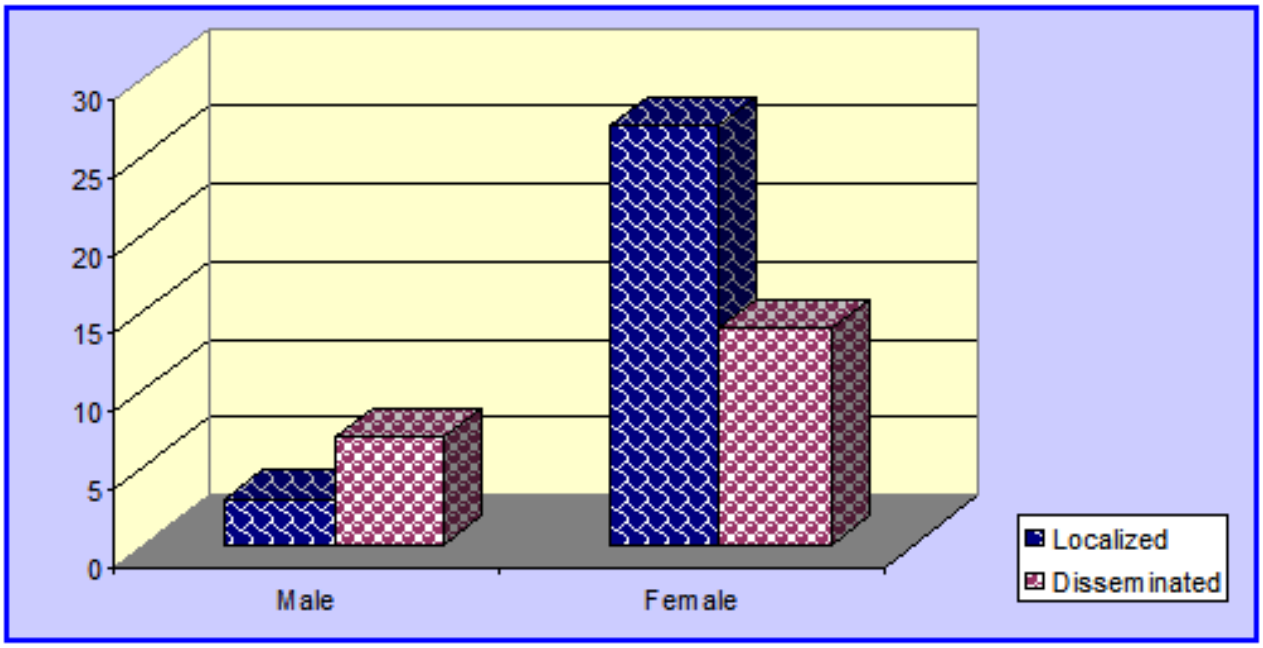
CONCLUSION

A total of 51 patients had DLE lesions during the study period with an incidence of 0.47 per 1000 cases attending dermatology OPD. The majority of our patients had disease onset at 3rd and 4th decade. Females outnumbered males in our study. Among male patients disseminated type was found more frequent than localized type. The distribution of lesion inferred that the majority of patient with lowerlimb and palms & soles involvement had complications like ulceration. 5.8 % of localized type and 17.6 % of disseminated type had SLE during the study period. But serious morbidity like lupus nephritis was observed in only one patient implying the benign nature of DLE. Cutaneous and systemic associations observed in our study were PLE, Hansen's disease, melasma, macular amyloid, vitiligo, systemic sclerosis and thyroid dysfunction. Squamous cell carcinoma was observed in two patients with disseminated lesion. Another interesting observation made was development of DLE lesion over herpes zoster site, an isomorphic phenomenon.

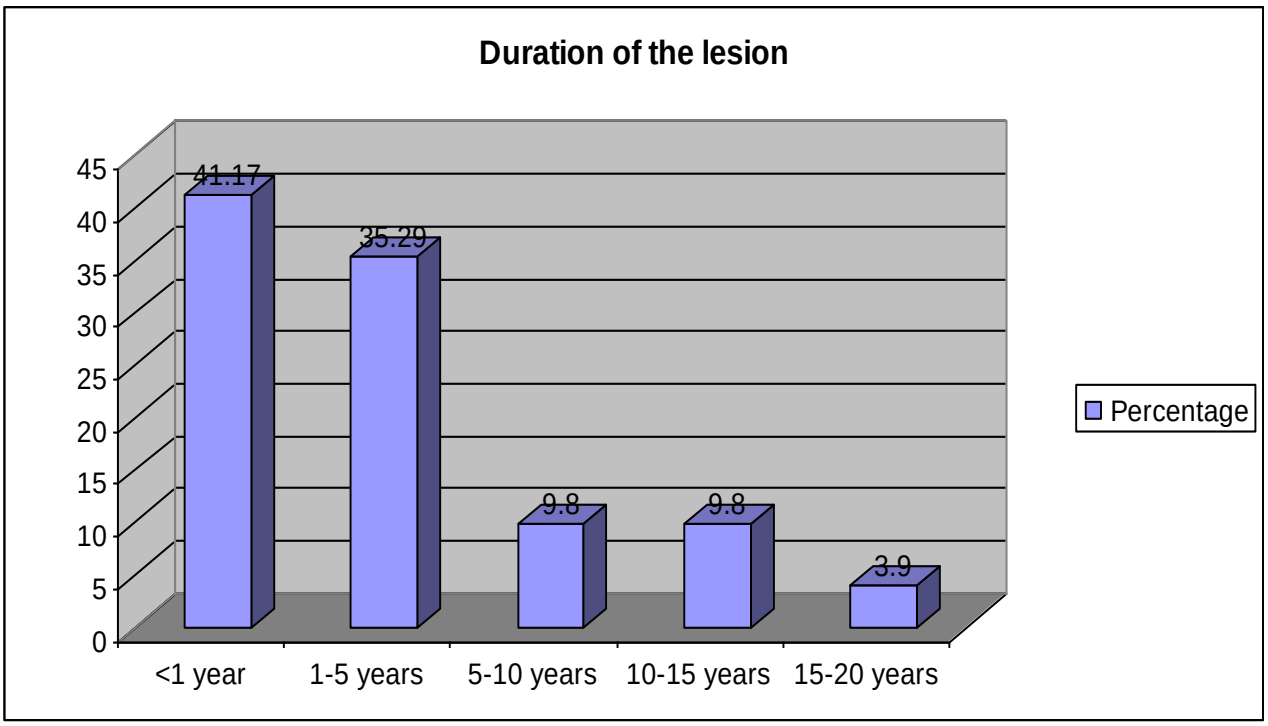

Clinical type of DLE
41.17%
21
58.82%
30
Localized
Disseminated


The age of onset
40
35
30
25
20
15
10
5
0
0
3.9
21.56
37.25
23.52
9.8
3.9
0-10
11-20
21-30
31-40
41-50
51-60
61-70

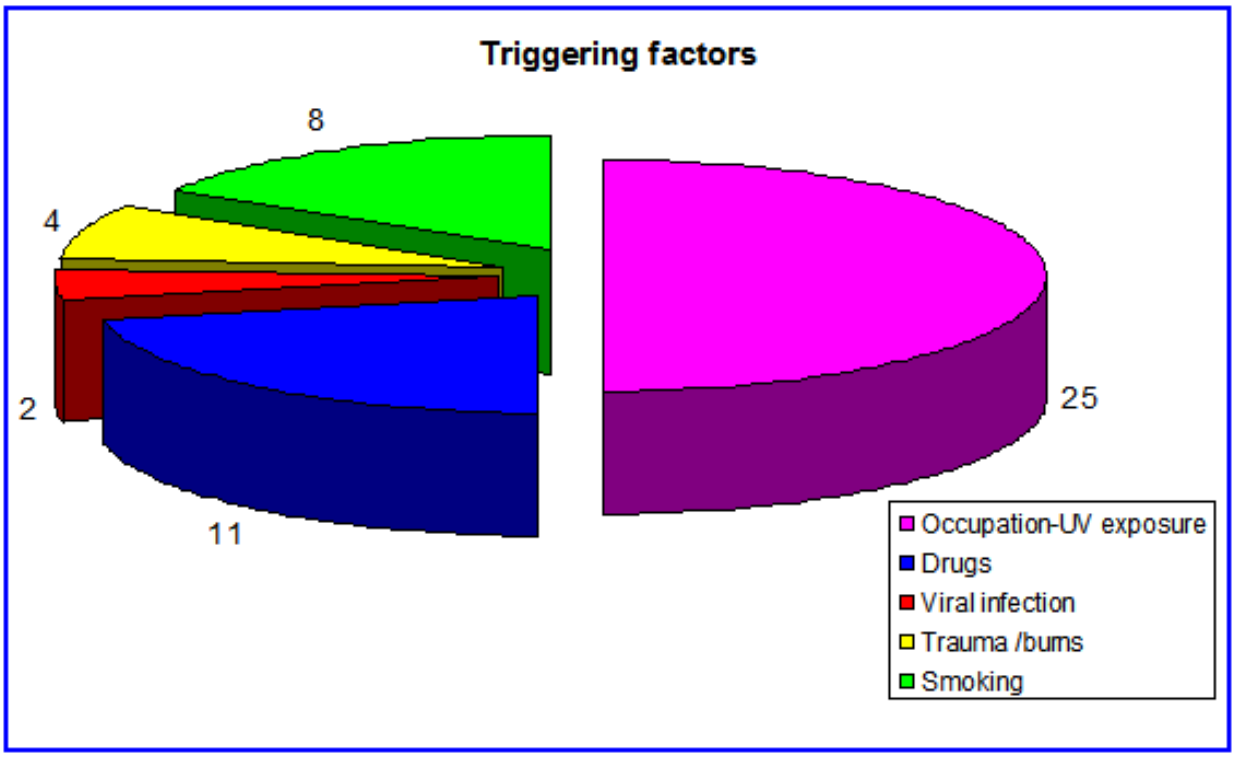
SEX DISTRIBUTION



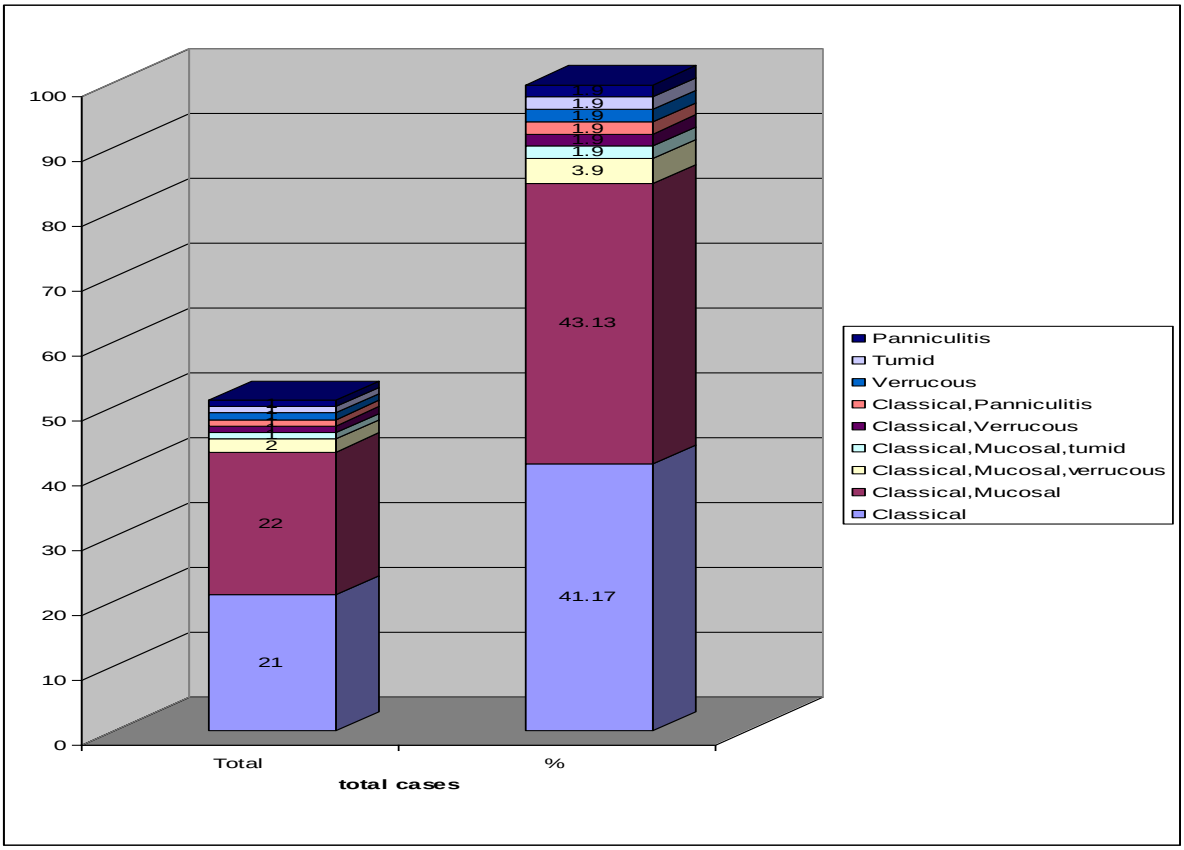
DURATION OF THE LESION

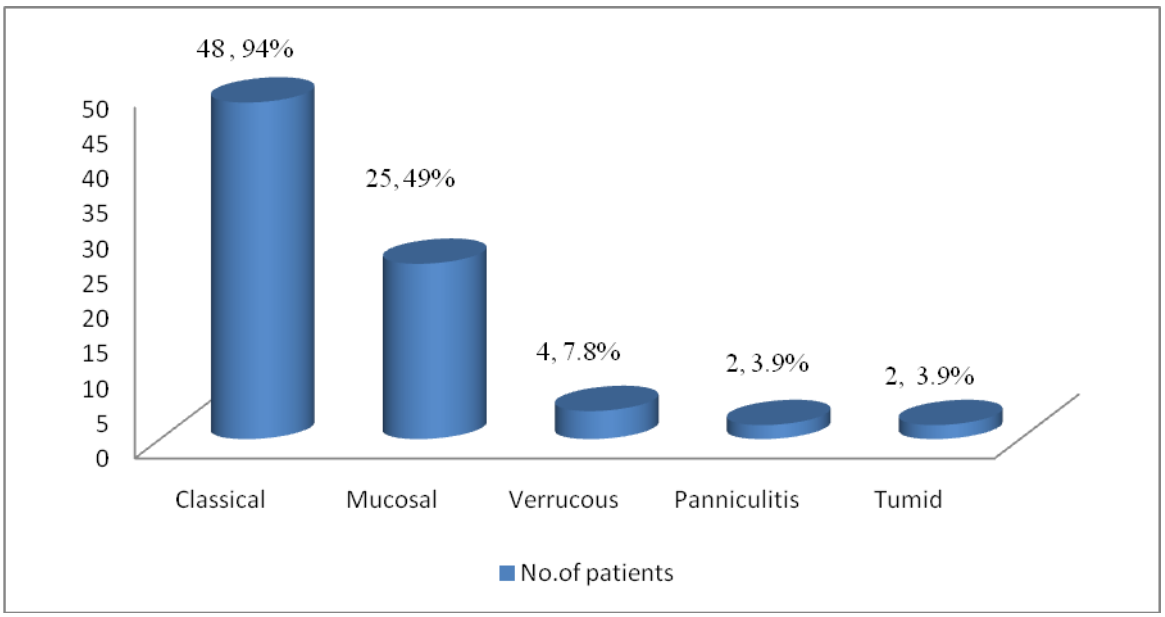


TRIGGERING FACTORS

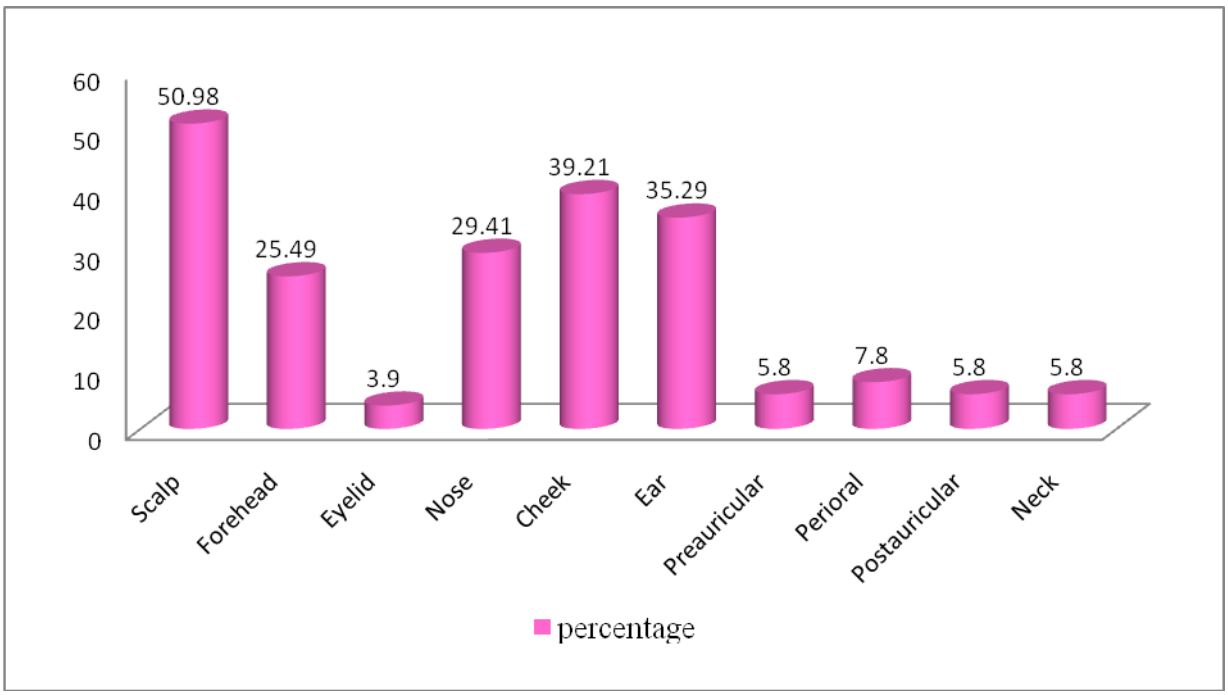


VARIANTS OF DLE

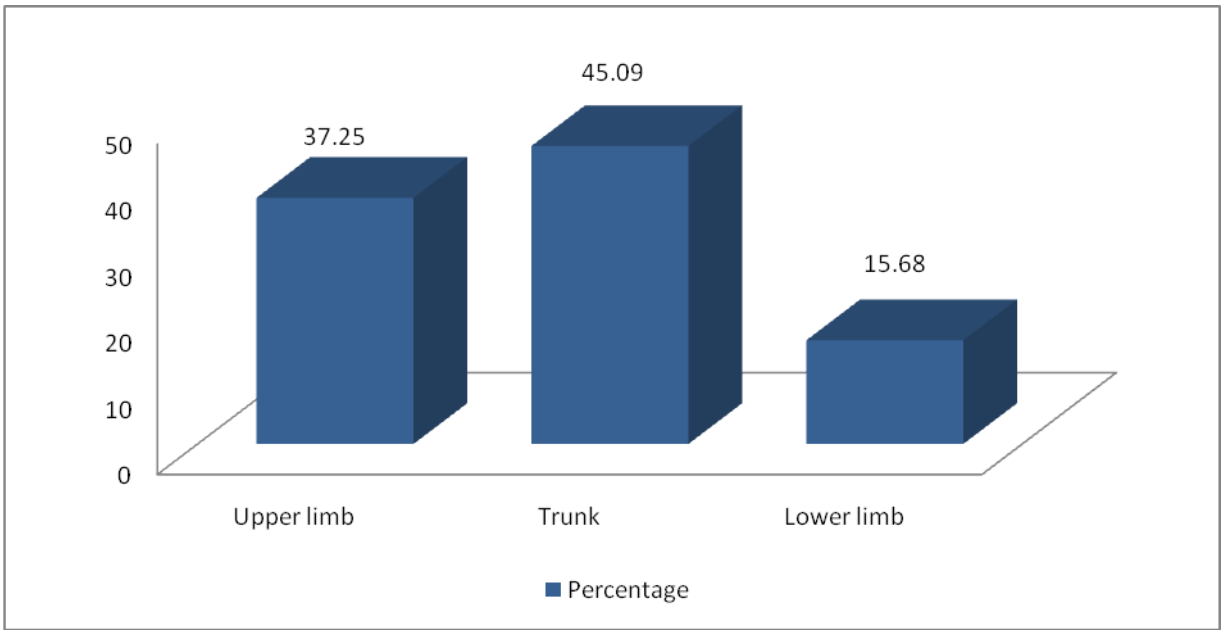


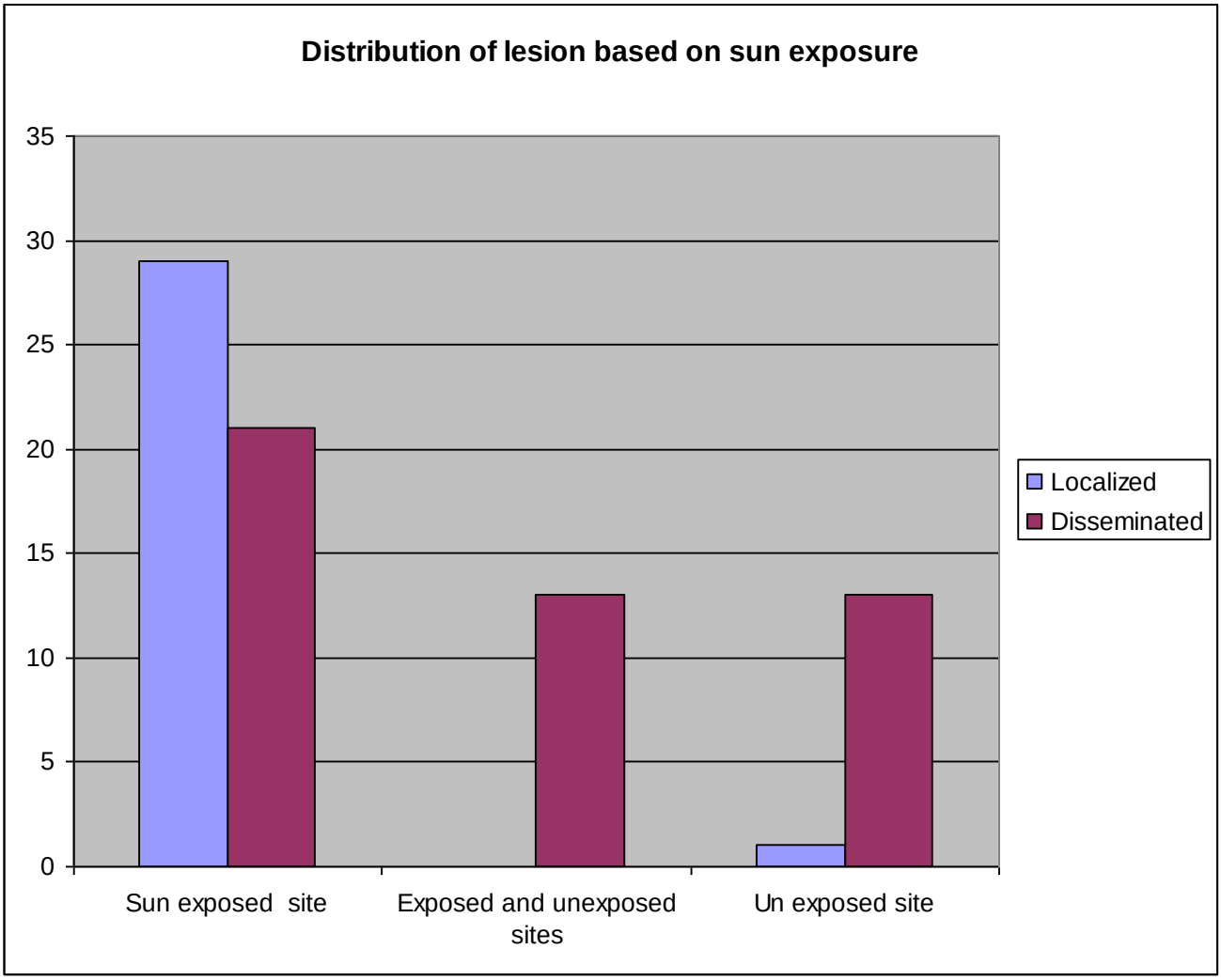


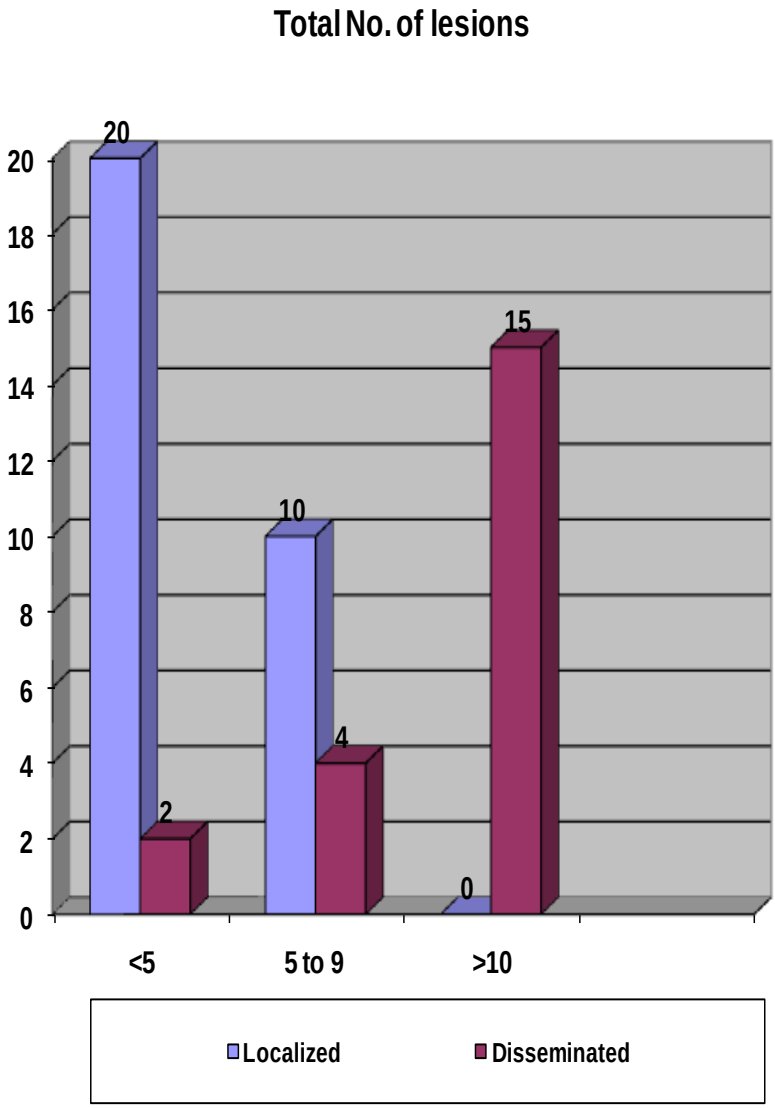
HEAD AND NECK INVOLVEMENT - SITES

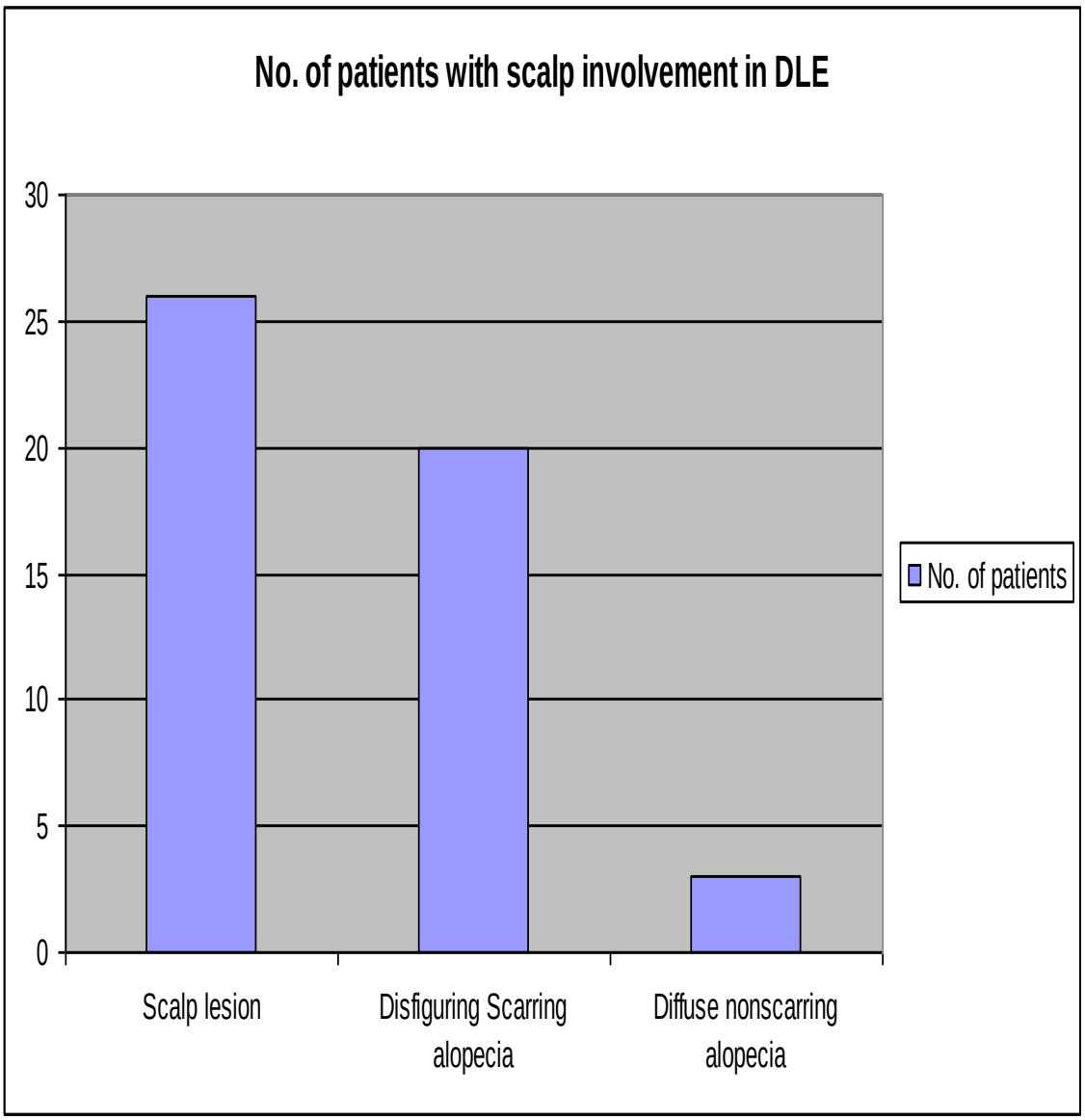


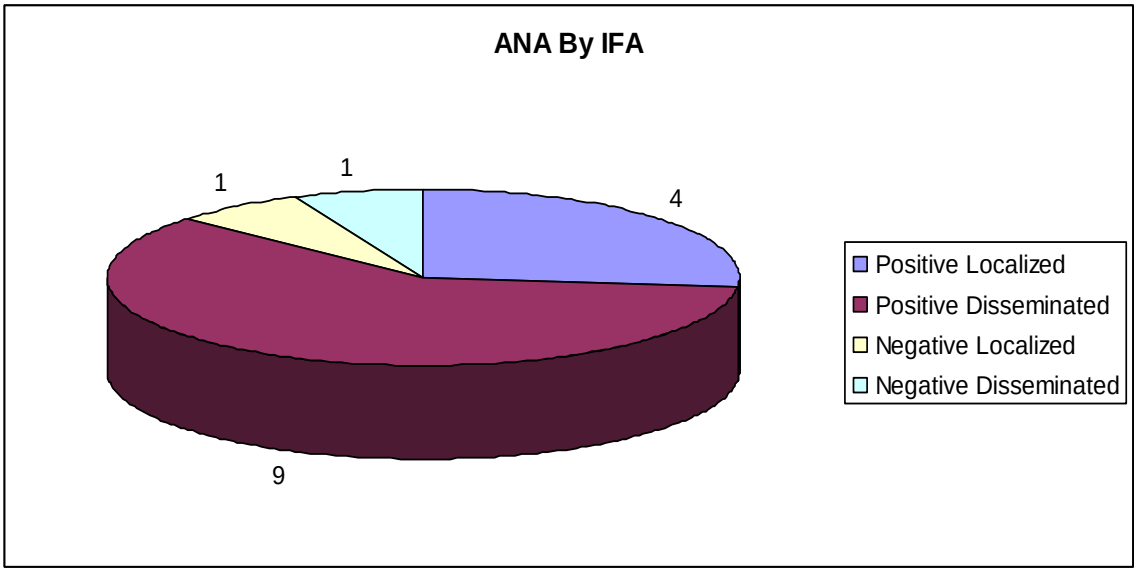
Involvement of sites other than head and neck

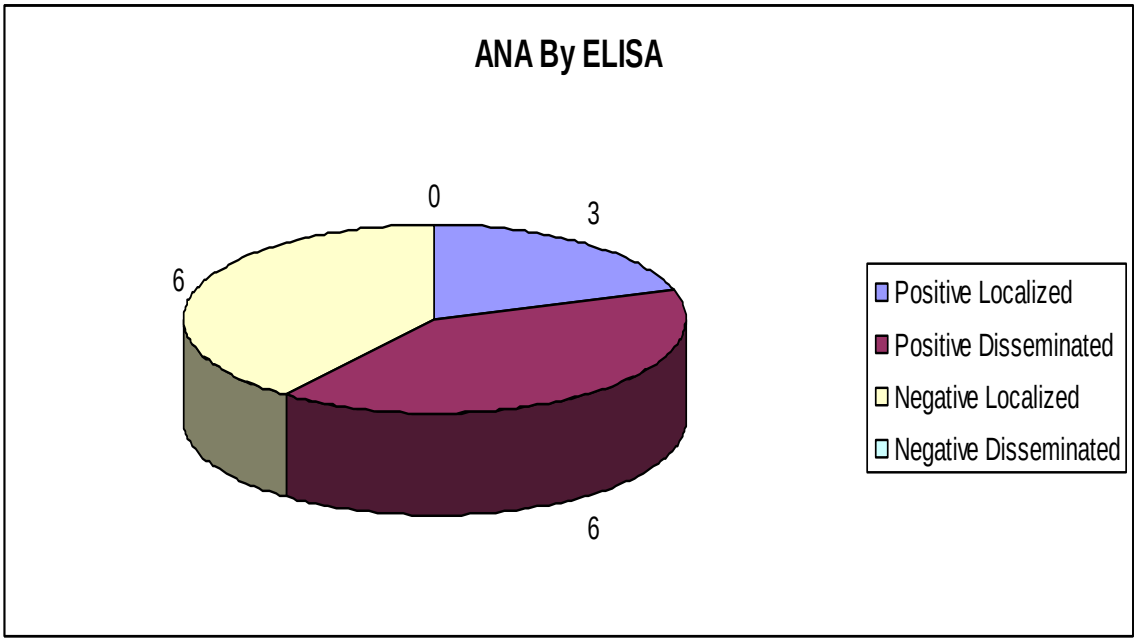


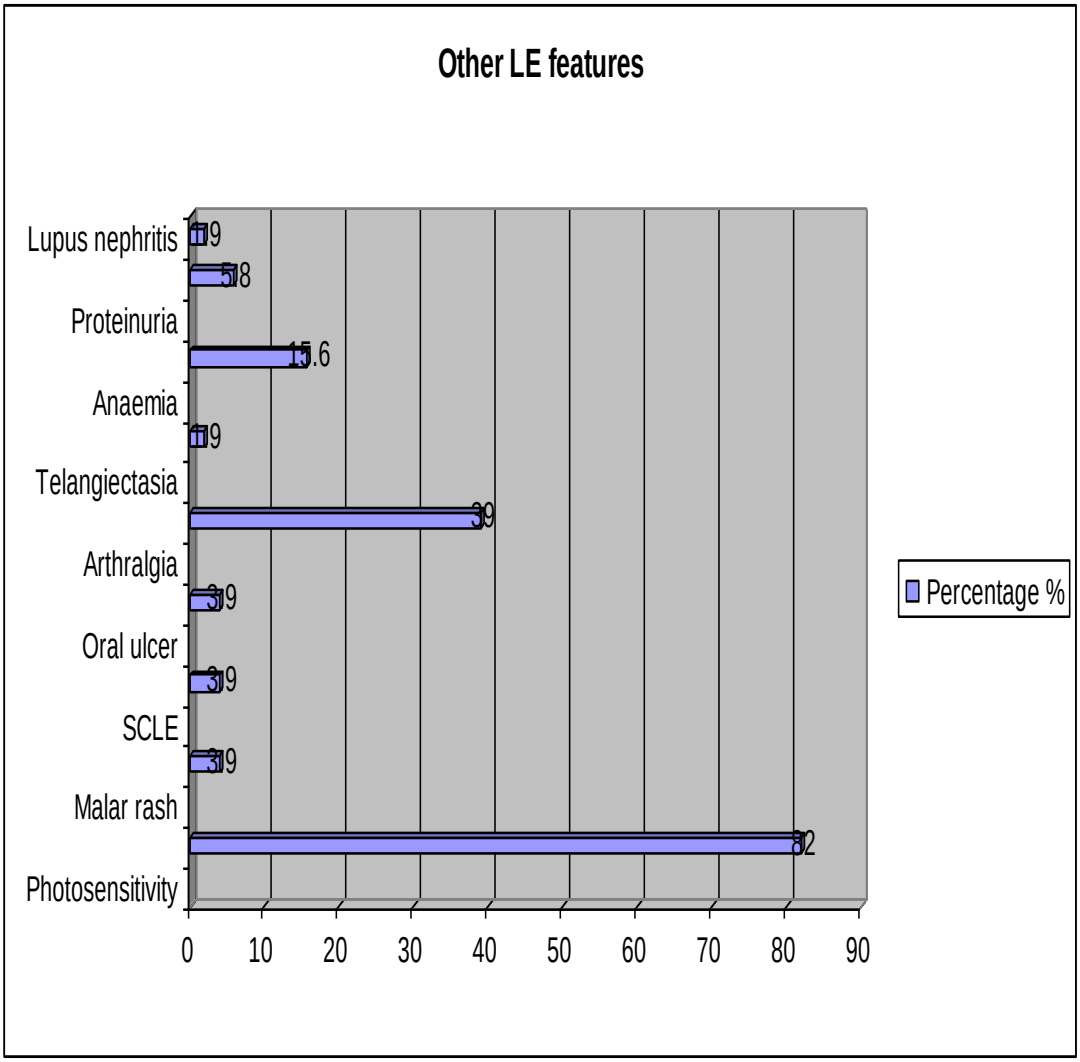

Distribution of lesion based on sun exposure
35
30
25
20
15
10
5
0
Sun exposed site
Exposed and unexposed sites
Un exposed site
Localized
Disseminated


Total No. of lesions
20
18
16
14
12
10
8
6
4
2
0
20
2
10
4
0
15
<5
5 to 9
>10
Localized
Disseminated


No. of patients with scalp involvement in DLE
30
25
20
15
10
5
0
Scalp lesion
Disfiguring Scarring alopecia
Diffuse nonscarring alopecia
No. of patients


ANA By IFA
1
1
4
9
Positive Localized
Positive Disseminated
Negative Localized
Negative Disseminated


ANA By ELISA
0
3
6
6
Positive Localized
Positive Disseminated
Negative Localized
Negative Disseminated


Other LE features
Lupus nephritis
Proteinuria
Anaemia
Telangiectasia
Arthralgia
Oral ulcer
SCLE
Malar rash
Photosensitivity
0
10
20
30
40
50
60
70
80
90
Percentage %

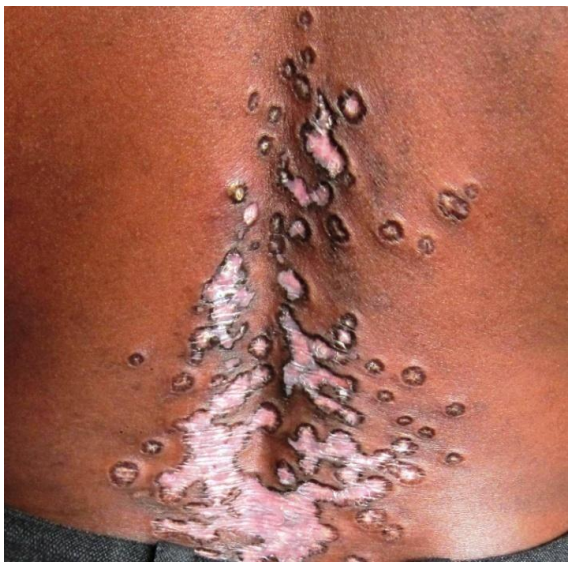
DLE ON FACE

DLE ON SCALP

CONCHA SIGN

DLE ON CHEST

LOWER BACK LESION



LOWER BACK LESION

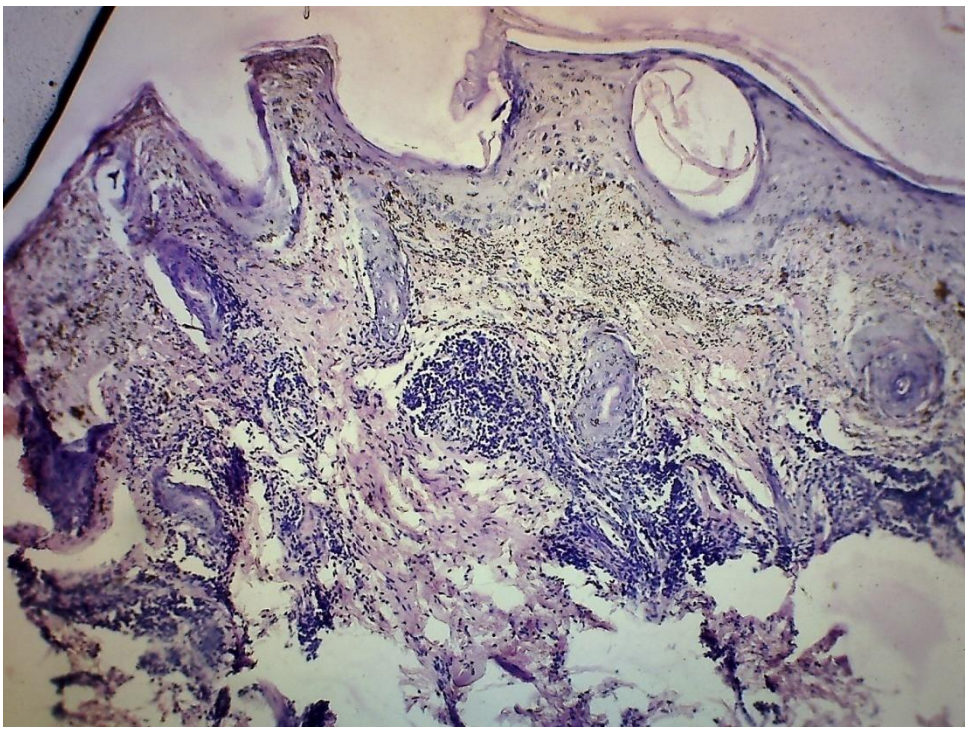
DLE LESION OVER FOREARM

DLE ON THIGHS

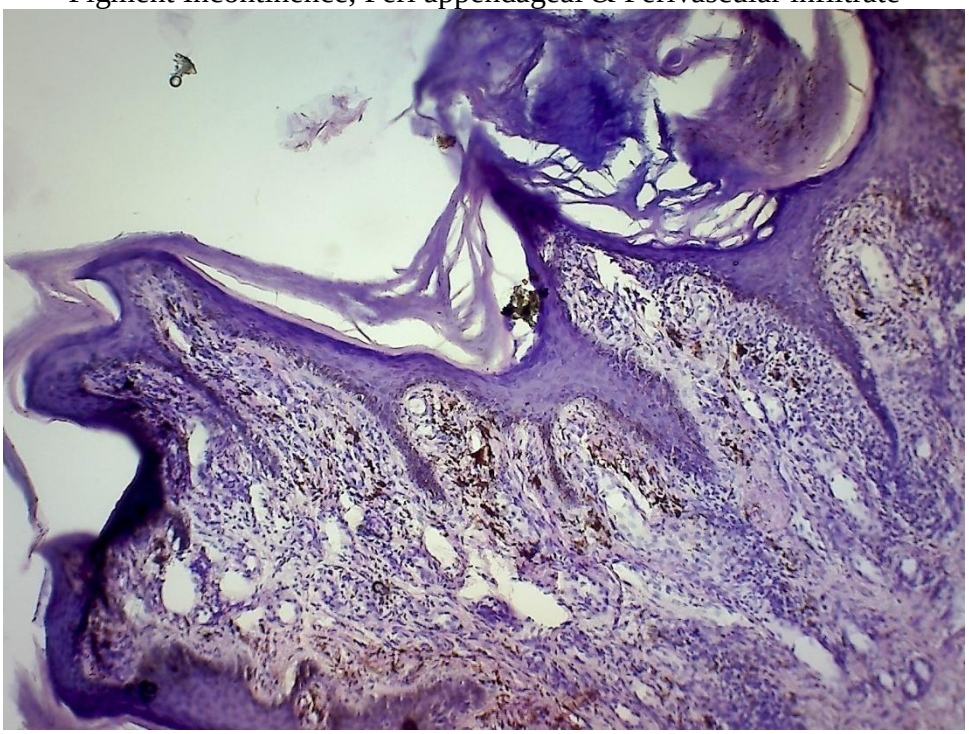
DLE LESION INVOLVING SOLE

INVOLVEMENT OF PALMS

HPE OF DLE



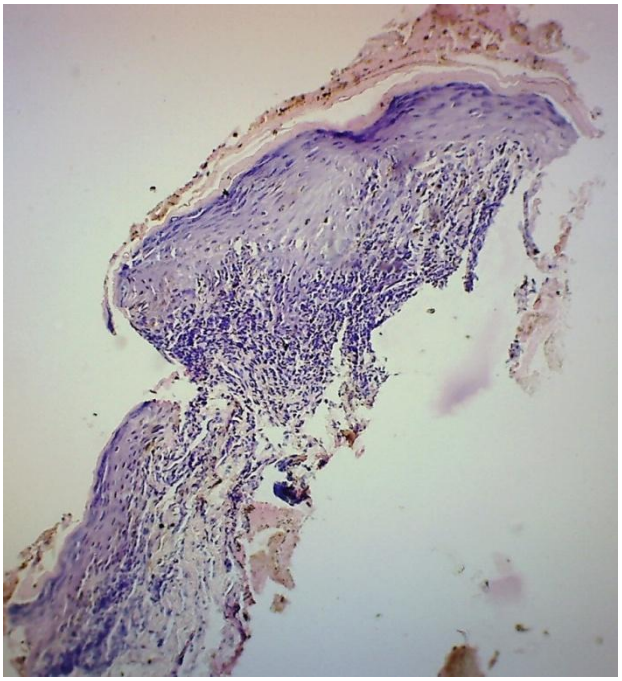
H & E, 10X Hyperkeratosis, Follicular plugging, Basal layer degeneration, Pigment Incontinence, Peri appendageal & Perivascular infiltrate



H & E, 10X

DISCOID LESION ON UPPER & LOWER LIP

HPE OF MUCOSAL DLE



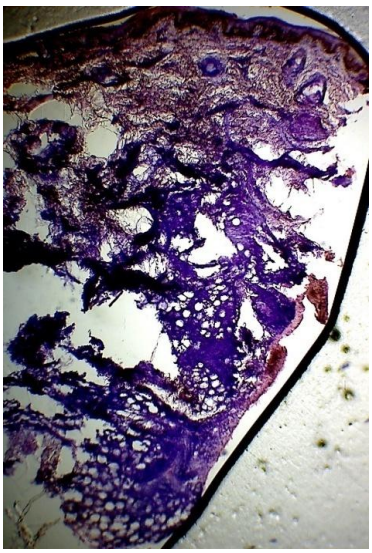
H & E, 10X Hyperkeratosis, Basal layer degeneration, Lymphocytic infiltrate

VERRUCOUS DLE

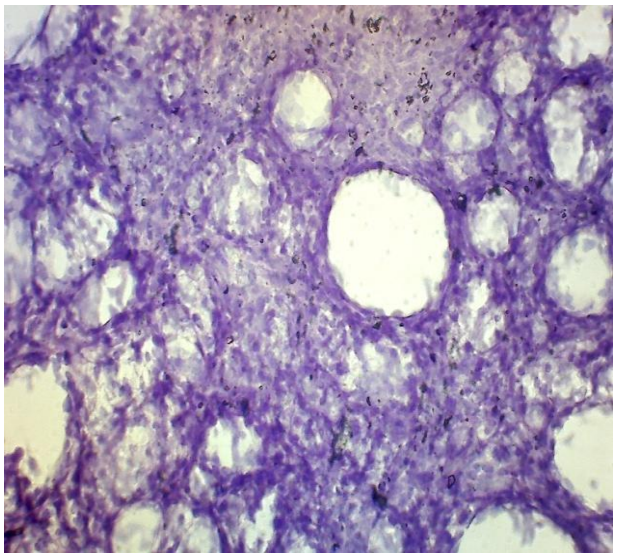
TUMID LE

LE PANNICULITIS INVOLVING SCALP & THIGH

HPE OF LE PANNICULITIS – MIXED PANNICULITIS



H & E, 5X

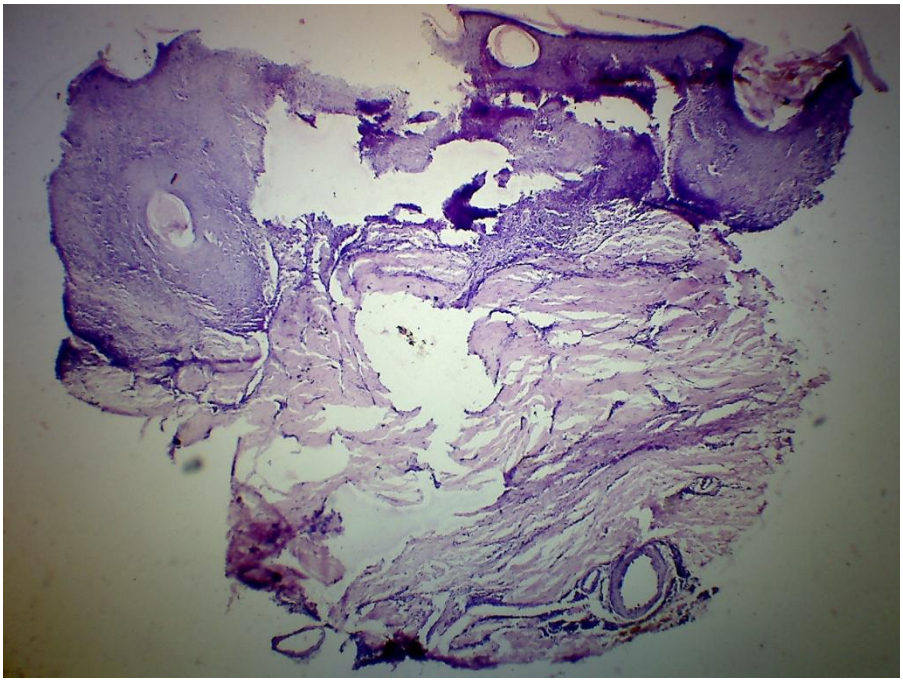


H & E, 40X

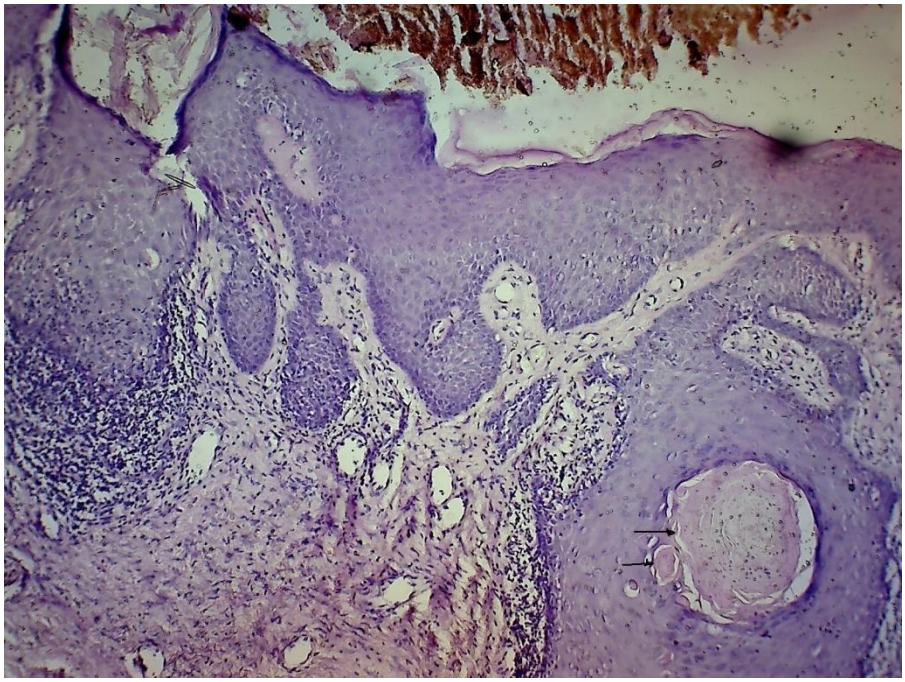
SQUAMOUS CELL CARCINOMA OVER DLE LESION ON ARM

SQUAMOUS CELL CARCINOMA OVER DLE LESION ON ELBOW

HPE OF SCC OVER DLE

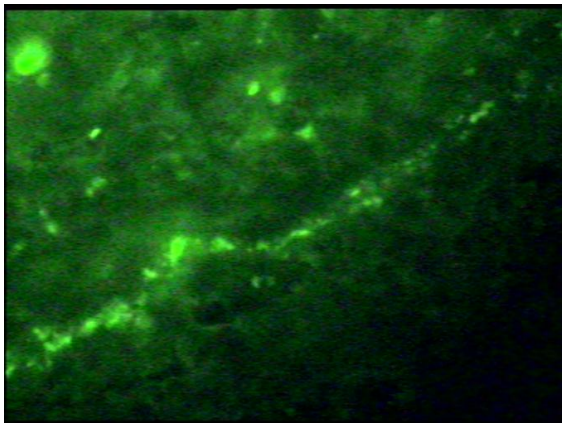


H & E, 5X

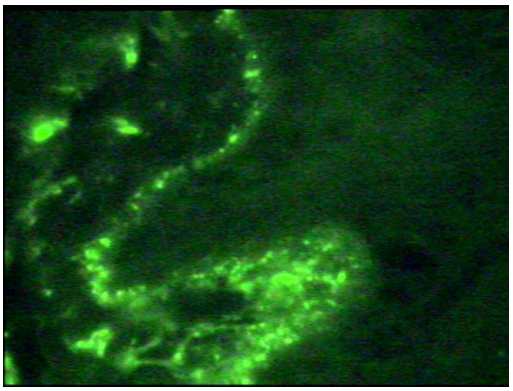


H & E, 10X Arrows – Horn Pearls, Individual cell Keratinization

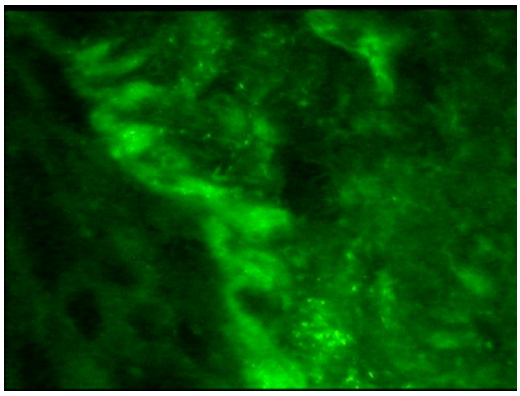
DIF



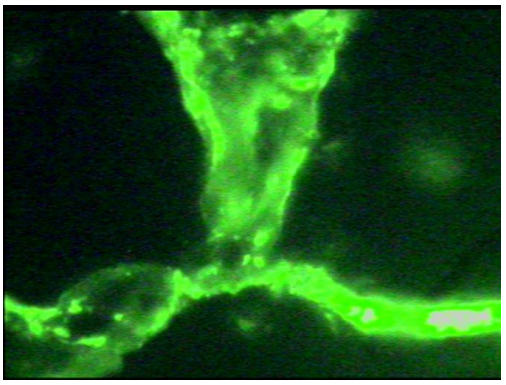
Deposition of IgG in LBT



Deposition of IgA in LBT



Deposition of IgM in Lesional skin



Deposition of Fibrinogen in Septae of fat

ULCERATION OVER DLE LESION ON LEGS

DLE LESION OVER HERPES ZOSTER SITE IN A PATIENT WITH DISSEMINATED DLE

BIBLIOGRAPHY

1. Smith CD, Cyr M. The history of lupus erythematosus, from Hippocrates to Osler. Rheum Dis Clin North Am1988;14:1-14.

2. Cazenave PLA, Schedel HE. Manual of the Diseases of the Skin. Burgess (trans). London, Henry Renshaw, 1852.

3. Hebra F. On Diseases of the Skin including the Exanthemata, Vol 1. Adams F (trans). London, The New Sydenham Society 1866.

4. Hargraves MM. Discovery of the LE cell and its morphology. Mayo Clin Proc 1969;44:579- 599.

5. Friou GJ. Antinuclear Antibodies: diagnostic significance and methods. Arthritis Rheum 1967;10:151-159

6. Arnett FC, Shulman LE. Studies in familial systemic lupus erythematosus. Medicine (Baltimore) 1976;55:313-322

7. Ravi K. Mallavarapu, MD, Edwin W. Grimsley, The History of Lupus Erythematosus.South Med J. 2007;100(9):896-898.

8. Durosaro BS, Davis MD, et al. Incidence of Cutaneous Lupus Erythematosus, 1965-2005: A Population-Based Study. Arch dermatol mar 2009;145(3):249-253.

9. Costner, Sontheimer. Lupus Erythematosus. In: Wolff K, Goldsmith LA, Katz SI, eds. Fitzpatrick's Dermatology in General Medicine, 7th edn. Philadelphia: McGraw-Hill; 2008;156(27):1515-1530

10. Damm J, Sonnischsen N. Clinical examinations of chronic lupus erythematosus. Dermatol Wochenschr 1964; 150: 268.

11. Goodfield MJ, Jones SK,Veale DJ. The connective tissue diseases.In: Stephen Breathnach, Christopher Griffiths and Neil Cox, Tony Burns,eds. Rook's textbook of dermatology. vol3, 8th ed.Sussex:Wiley-Blackwell; 2010;51.4-19

12. Millard TP, Kondeatis E, Vaughan RW et al. Polymorphic light eruption and the HLA DRB1*0301 extended haplotype are independent risk factors for cutaneous lupus erythematosus. Lupus 2001; 10: 473–9.

13. A Osmola et al. Genetic background of cutaneous forms of lupus erythematosus: update on current evidence. J. Appl. Genet. 45(1), 2004, pp. 77-86.

14. Werth V.P., Zhang W., Dortzbach K., Sullivan K. (2000). Association of a promoter polymorphism of tumor necrosis factor-alpha with SCLE and distinct photoregulation of transcription. J. Invest. Dermatol. 115(4): 726-730.

15. Bielsa I, Herrero C, Ercilla G et al. Immunogenetic findings in cutaneous lupus erythematosus. J Am Acad Dermatol 1991; 25: 251–7.

16. Urnovitz H.B., Murphy W.H. (1996). Human endogenous retroviruses: nature, occurrence and clinical implications in human disease. Clinical Microbiology Reviews72-99

17. Casciola-Rosen L, Rosen A: Ultraviolet light-induced keratinocyte apoptosis: A potential mechanism for the induction of skin lesions and autoantibody production in LE. Lupus 6:175, 1997

18. Meller S et al: Ultraviolet radiation-induced injury, chemokines, and leukocyte recruitment: An amplification cycle triggering cutaneous lupus erythematosus. Arthritis Rheum 52:1504, 2005

19. Yung RL et al: Mechanism of drug-induced lupus. I. Cloned Th2 cells modified with DNA methylation inhibitors in vitro cause autoimmunity in vivo. J Immunol 154:3025, 1995

20. Grundwald M, David M, Feuerman EJ. Appearance of lupus erythematosus in a patient with lichen planus treated by isoniazid. Dermatologica 1982; 162:172–7.

21. Burns DA, Sarkany I. Penicillamine-induced discoid lupus erythematosus. Clin Exp Dermatol 1979; 4: 389–92.

22. Alexander S. Lupus erythematosus in two patients after griseofulvin treatment of Trichophyton rubrum infection. Br J Dermatol 1962; 74: 72–4.

23. Lupton GP. Discoid lupus erythematosus occurring in a smallpox vaccination scar. J Am Acad Dermatol 1987; 89: 688–90.

24. Arthur B. Kern, M.D.; Bencel L. Schiff.Discoid Lupus Erythematosus Following TraumaReport of Cases and Analysis of a Questionnaire.Arch Dermatol. 1957;75(5):685-688.

25. Poole BD, Scofield RH, Harley JB, James JA. Epstein-Barr virus and molecular mimicry in systemic lupus erythematosus. Autoimmunity. 2006 Feb;39(1):63-70

26. Valente RM,et al.Toll-like receptor 7 stimulates the expression of Epstein-Barr virus latent membrane protein 1. PLoS One. 2012;7(8):e43317

27. Anette Holck Draborg, Karen Duus, and Gunnar Houen. Epstein-Barr Virus and Systemic Lupus Erythematosus. Clin Dev Immunol. 2012; 370516.

28. Rahman P, Gladman DD, Urowitz MB: Smoking interferes with efficacy of antimalarial therapy in cutaneous lupus. J Rheumatol 25:1716, 1998

29. Hardy CJ et al: Smoking history, alcohol consumption, and systemic lupus erythematosus: A case-control study. Ann Rheum Dis 57:451, 1998

30. Jewell ML, McCauliffe DP: Patients with cutaneous lupus erythematosus who smoke are less responsive to antimalarial treatment. J Am Acad Dermatol 42:983, 2000

31. Gill MA et al: Blood dendritic cells and DC-poietins in systemic lupus erythematosus. Hum Immunol 63:1172, 2002

32. Braunstein I, Klein R, Okawa J, Werth VP. The IFN-regulated gene signature is elevated in SCLE and DLE and correlates with CLASI score. Br J Dermatol 2012

33. Pascual V, Banchereau J, Palucka AK: The central role of dendritic cells and interferon-alpha in SLE. Curr Opin Rheumatol 15:548, 2003

34. Agnello V.: Lupus diseases associated with hereditary and acquired deficiencies of complement. Springer Semin Immunopathol 1986; 9(2-3):161-178.

35. Bowness P., Davies K.A., Norsworthy P.J., et al: Hereditary C1q deficiency and systemic lupus erythematosus. QJM 1994; 87:455-464.

36. Walport M.J., Davies K.A., Morley B.J., et al: Complement deficiency and

autoimmunity. Ann N Y Acad Sci 1997; 815:267-281.

37. Atkinson J.P., Schifferli J.A.: Complement system and systemic lupus erythematosus. Lupus: Molecular and Cellular Pathogenesis, Totowa, NJ: Humana Press; 1999.

38. Chandrashekar L. Update on cutaneous lupus erythematosus. Indian J Dermatol Venereol Leprol 2012;78:129-32

39. Palucka AK et al: Cross-regulation of TNF and IFN-alpha in autoimmune diseases. Proc Natl Acad Sci U S A 102:3372, 2005

40. Mikita N, Ikeda T, Ishiguro M, Furukawa F. Recent advances in cytokines in cutaneous and systemic lupus erythematosus. J Dermatol 2011;38:839-49

41. Zahn S, Rehkämper C, Ferring-Schmitt S, Bieber T, Tüting T, Wenzel J. Interferon-á stimulates TRAIL expression in human keratinocytes and peripheral blood mononuclear cells: Implications for the pathogenesis of cutaneous lupus erythematosus. Br J Dermatol 2011;165:1118-23

42. Antiga E, Del Bianco E, Difonzo E, Fabbri P, Caproni M. Serum levels of the regulatory cytokines transforming growth factor-β and interleukin-10

are reduced in patients with discoid lupus erythematosus. Lupus 2011;20:556-60

43. Hahn B.H, Betty P.Tsao. Pathogenesis of Systemic Lupus Erythematosus. In : Gary S. Firestein, Ralph C. Budd, Edward D. Harris et al,eds. Kelley's Textbook of Rheumatology,vol1.8th ed. Philadelphia: WB Saunders; 2009;(11);1238

44. Hahn B.H., Ebling F., Singh R.R., et al: Cellular and molecular mechanisms of regulation of autoantibody production in lupus. Ann N Y Acad Sci 2005; 1051:433-441

45. Wenzel J et al: Scarring skin lesions of discoid lupus erythematosus are characterized by high numbers of skin-homing cytotoxic lymphocytes associated with strong expression of the type I interferon-induced protein MxA. Br J Dermatol 153:1011, 2005

46. Sawalha AH, Harley JB: Antinuclear autoantibodies in systemic lupus erythematosus. Curr Opin Rheumatol 16:534, 2004

47. Kangle S, Amladi S, Saswant S. Scaly signs in Dermatology. Indian J Dermatol Venereol Leprol 2006 ;72 :161-4

48. Paramsothy Y, Lawrence CM. 'Tin-tack' sign in localized pemphigus foliaceus. Br J Dermatol 1987; 116: 127–9.

49. Shuster S. A simple sign of discoid lupus erythematosus. Br J Dermatol 1981; 104:350–1.

50. JeffreyPCallen,MD.DiscoidLupusErythematosus .emedicine.medscape.com/article/1065529-overview

51. Callen JP . Chronic cutaneous lupus erythematosus. Clinical, laboratory, therapeutic, and prognostic examination of 62 patients. Arch Dermatol 1982; 118: 412-416.

52. Jeffrey P Callen, MD. Subacute Cutaneous Lupus Erythematosus (SCLE).emedicine.medscape.com/article/1065657-overview

53. Crocker HR. Diseases of the Skin: Their Description, Pathology, Diagnosis and Treatment.Philadelphia: Blakiston, 1888.

54. Nagy E, Balogh E. Bullous form of chronic discoid erythematodes accompanied by LE-cell symptoms. Dermatologica 1961; 122: 6–10.

55. Green JJ, Baker DJ. Linear childhood discoid lupus erythematosus following the lines of Blaschko: a case report with review of the linear manifestations of lupus erythematosus. Pediatr Dermatol 1999; 16: 128–33.

56. Behcet PE. Hypertrophic lupus erythematosus. Arch Dermatol Syphilol 1940;42:211

57. Uitto J, et al. Verrucous lesions in patient with discoid lupus erythematosus: clinical, histopathological, and immunofluorescence studies. Br J Dermatol 1978; 98: 507

58. Lee LA. Lupus erythematosus. In : Bolognia J, et al, eds. Dermatology, 2nd ed., London: Mosby, 2008: 561

59. James, William; Berger, Timothy; Elston, Dirk (2005). Andrews' Diseases of the Skin: Clinical Dermatology. (10th ed.). Saunders. Page 158.

60. Santa Cruz DJ, Uitto J, Eisen A Z, Prioleau P G. Verrucous lupus erythematosus: Ultrastructural studies on a distinct variant of chronic discoid lupus Erythematosus.J Am Acad Dermatol.1983;9:82-90

61. Annegret K,Sontheimer R,Ruzicka T.Clinical manifestations of cutaneous lupus Erythematosus.In: cutaneous lupus Erythematosus. Annegret Kuhn, Percy Mario Lehmann eds. 1st ed. Heidelberg;springer-verlag; 2004; pp70-74

62. Marks R, Levene GM. Discoid lupus erythematosus and lupus Erythematosus profundus in a child. Clin Exp Dermatol 1976; 1: 187.

63. de Bandt M, Meyer O, Grossin M *et al.* Lupus mastitis heralding systemic lupus erythematosus with anti-phospholipid syndrome. J Rheumatol 1993; 20:1217–20

64. Sheehan-Dare RA, Cunliffe WJ. Severe periorbital oedema in association with lupus erythematosus profundus. Clin Exp Dermatol 1988; 13: 406–7.

65. Inuzuka, M, Tomita K, Tokura K, Takigawa M. Lupus erythematosus profundus with unusual skin manifestation: subcutaneous nodules coexisting with eyelid plaques. J Dermatol 2001; 28: 437–41.

66. Dekle CL, Mannes KD, Davis LS, Sangueza OP. Lupus tumidus. J Am Acad Dermatol. 1999 Aug;41(2 Pt 1):250-3.

67. Kuhn A, Richter-Hintz D,et al. Lupus erythematosus tumidus--a neglected subset of cutaneous Lupus erythematosus: report of 40 cases. Arch Dermatol. 2000 Aug;136(8):1033-41.

68. Vieira V, Del Pozo J, et al.Lupus erythematosus tumidus: a series of 26 cases. Int J Dermatol. 2006 May;45(5):512-7

69. Millard L.G, Rowell N.R. Chilblain lupus erythematosus (Hutchinson) A Clinical and laboratory study of 17 patients. Br J Dermatol.1978 May;

98(5):497-506

70. Mascaro JM, Herrero C,Hausmann G. Uncommon cutaneous manifestations of lupus erythematosus. Lupus.1997;6:122-31.

71. Franceschini F et al: Chilblain lupus erythematosus is associated with antibodies to SSA/Ro. Lupus 8:215, 1999

72. Viguier M et al: Clinical and histopathologic features and immunologic variables in patients with severe chilblains. A study of the relationship to lupus erythematosus. Medicine (Baltimore) 80:180, 2001

73. Richard D Sontheimer et al. Lupus-specific skin disease(cutaneous LE).In: Dubois' Lupus Erythematosus. Daniel Jeffrey Wallace, Bevra Hannahs Hahn et al,eds. 7th ed. Philadelphia ; Lippincott Williams & Wilkins: 2007;30:594

74. Lourencxo S L, et al. Lupus erythematosus: Clinical and histopathological study of oral manifestations and immunohistochemical profile of the inflammatory infiltrate. J Cutan Pathol 2007; 34: 558–564

75. Burge SM, Frith PA, Juniper RP, Wojnarowska F. Mucosal involvement in systemic and chronic cutaneous lupus erythematosus. Br J Dermatol 1989; 121: 727.

76. Jonsson R, Hieden G, Westberg NG, Nyberg G. Oral mucosal lesions in systemic lupus erythematosus: a clinical, histopathological and immunopathological study. J Rheumatol 1984; 11: 38.

77. Schiodt M. Oral discoid lupus erythematosus. III. A histopathologic study of sixty-six patients. Oral Surg Oral Med Oral Pathol 1984; 57: 281

78. Inaloz HS, Chowdhury M, Motley R et al. Lupus erythematosus/lichen planus overlap syndrome with scarring alopecia. J Eur Acad Dermatol Venereol 2000; 15: 171-4.

79. Jablonska S, Blaszozyk M. Lupus erythematosus. What's new? J Eur Acad Dermatol Venereol 2000; 15: 103-5.

80. Pittellcow MR, Daould MS. Lichen planus. In: Wolff K, Goldsmith LA, Katz SI, eds. Fitzpatrick's Dermatology in General Medicine, 7th edn. Philadelphia: McGraw-Hill; 2008. p.250.

81. Galliano D, Cardesi E, Gondolfo S et al. Keratotic lesions of the oral cavity. Notes on histopathologic differential diagnosis in leukoplakia, lichen planus, lupus erythematosus. Cases investigation. Minerva Stomatol 1989; 38: 481-7.

82. Grasbe S, Kolde G. Coexisting lichen planus and subacute cutaneous lupus erythematosus. Clin Exp Dermatol 1995; 20: 249-54.

83. Tursen U, Oz O, Ikizoglu G et al. A case of lichen planus lupus erythematosus overlap syndrome with eyelid involvement. Eur J Ophthalmol 2002; 12: 244-6

84. Kint A, van Herpe L. Ungual anomalies in lupus erythematosus discoides. Dermatologica 1976; 153: 298–302

85. Tosti A, Tosti G, Giovannini A. Discoid lupus erythematosus solely involving the eyelids: report of three cases. J Am Acad Dermatol 1987; 16: 1259–60.

86. Rothfield NF. Cutnaeous manifestations of multisystem diseases. Chapter 171:2137-2141

87. Jaworsky, C. Connective tissue diseases. In Lever's Histopathology of the Skin. Philadelphia, PA, Raven Publsihers, 1997:253-61.

88. Brenner EH, Shock JF. Proptosis secondary to systemic lupus erythematosus. Arch Ophthalmol 1974:215;2019-20.

89. Klauder JV, De Long P. Lupus erythematosus of the conjunctiva, eyelids

and lid margins. Arch Ophthalmol 1932;7: 856-867.

90. Raizman MB, Baum J. Discoid lupus keratitis. Arch Ophthalmol 1989;107:545-547.

91. Foster RE, Lowder CY, Meisler DM, et al. An unusual ocular manifestation of discoid lupus erythematosus. Cleve Clin J Med 1994;61:232-237.

92. Jerdan MS, Hood AF, Moore GW, Callen JP. Histopathologic comparison of subsets of lupus erythematosus. Arch Dermatol 1990;126:52-5.

93. Callen JP, Fowler JF, Kulick K. Serologic and clinical features of patients with discoid lupus erythematosus. J Am Acad Dermatol 1985;13:748-55.

94. Burge SM, Frith PA, Millard PR, Wojnarowska IF. External ocular findings in lupus erythematosus: a clinical and immunopathological study. Br. J Ophthalmol 1990;74:163-167.

95. Williams WL, Ramos-Caro FA. Acute periorbital mucinosis in discoid lupus erythematosus. J Am Acad Dermatol 1999; 41: 871–3.

96. Wilson C.L., Burge S.M., Dean D. and Dawber R.P.R., Scarring alopecia in discoid lupus erythematosus. Br J Dermatol 1992; 126: 307–314.

97. Fabbri P, Amato L et al. Scarring alopecia in discoid lupus erythematosus: a clinical, histopathologic and immunopathologic study. Lupus. 2004;13(6):455-62.

98. Werth VP, White WL, Sanchez MR. Incidence of alopecia areata in lupus erythematosus. Arch Dermatol 1992; 128: 368–71.

99. Trapl J, Sabatova M. Lupus erythematosus and parotitis. Dermatol Wochenschr 1960; 142: 817–9.

100. Nelson CT. Discoid lupus, reticulate livedo of legs, cryoglobulinemia. Arch Dermatol 1959; 80: 497–8.

101. Van der Meer-Roosen CH, Maes EPJ, Faber WR. Cutaneous lupus Erythematosus and autoimmune thyroiditis. Br J Dermatol 1979; 101: 91–2.

102. Wojnarowska F. Simultaneous occurrence in identical twins of discoid lupus erythematosus and polymorphic light eruption. J R Soc Med 1983; 76: 791–2.

103. Nyberg F et al. Occurrence of polymorphous light eruption in lupus Erythematosus. Br J Dermatol 1997 Feb;136(2):217-221

104. T P Millard et al. Polymorphic light eruption and the HLA DRB1*0301

extended haplotype are independent risk factors for cutaneous lupus Erythematosus. Lupus. 2001;10(7):473-9.

105. Jeffrey P. Callen M.D.* Discoid Lupus Erythematosus in a Patient with Vitiligo and Autoimmune Thyroiditis. Int J Dermatol 1984;23(3):203-204

106. Sasaki T, Nakajima H. Systemic sclerosis (scleroderma) associated with discoid lupus erythematosus. Dermatology. 1993;187(3):178-81.

107. Jaworsky C. Connective Tissue Diseases. In: David E. Elder et al, eds Lever's Histopathology of the Skin. 9th ed. Philadelphia. Lippincott Williams & Wilkins. 2005;(10):294-305

108. Panet-Raymond G, Johnson WC. Lupus erythematosus and polymorphous light eruption. Arch Dermatol 1973;108:785

109. D.H. McGibbon. Subcutaneous Fat.In: Stephen Breathnach, Christopher Griffiths,Neil Cox, Tony Burns,eds. Rook’s textbook of dermatology. vol3, 8th ed. Sussex:Wiley-Blackwell; 2010;46.25-26.

110. Sanchez NP, Peters MS, Winkelmann RK. The histopathology of lupus erythematosus panniculitis. J Am Acad Dermatol 1981; 5:673-680

111. Mcnutt S N, Moreno A,Contreras F. Inflammatory Diseases of the Subcutaneous Fat. In: David E. Elder et al, eds Lever's Histopathology of the Skin. 9th ed. Philadelphia. Lippincott Williams &

Wilkins.2005;(20):532-3

112. Macrene R. Alexiades-Armenakas, et al. Tumid lupus erythematosus: Criteria for classification with immunohistochemical analysis. Arthritis Rheum. 2003 Aug 15;49(4):494-500.

113. Peng S.L., Craft J:Antinuclearantibodies.In: Harris E.D., Budd R.C., Firest ein G.S., etal (eds). Kelley'sTextbookofRheumatology, Philadelphia: WB Saunders; 2005:311-331.

114. David F. Keren. Antinuclear antibody testing. Clin Lab Med 22 (2002) 447–474

115. Kavanaugh A., Tomar R., Reveille J., et al: Guidelines for clinical use of the antinuclear antibody test and tests for specific autoantibodies to nuclear antigens. American College of Pathologists. Arch Pathol Lab Med 2000; 124:71-81

116. Peng S.L., Craft J.: Antinuclear antibodies. In : Gary S. Firestein, Ralph C. Budd, Edward D. Harris et al,eds. Kelley's Textbook of Rheumatology,vol1.8th ed. Philadelphia: WB Saunders; 2009;742-746.

117. Jacyk WK, Damisah M (1979). Discoid lupus erythematosus in the Nigerians. Br. J. Dermatol. 100: 131-135.

118. Koskenmies S, Jarvinen TM, Onkamo P, Panelius J, Tuovinen U,Hasan T, Ranki A, Saarialho-Kere U (2008). Clinical and laboratory characteristics of Finnish lupus erythematosus patients with cutaneous manifestations. Lupus 17: 337-347.

119. Callen JP (1982). Chronic cutaneous lupus erythematosus. Clinical, laboratory, therapeutic, and prognostic examination of 62 patients. Arch Dermatol. 118: 412-416.

120. Insawang M, Kulthanan K, et al. Discoid lupus erythematosus: Description of 130 cases and review of their natural history and clinical course. Journal of Clinical Immunology and Immunopathology 2010 Apr; 2(1):1-8.

121. Beck JS, Rowell NR. Discoid lupus erythematosus. QJM 1966; 35: 119–36.

122. Prystowsky SD, Gilliam JN. Discoid lupus erythematosus as part of a larger disease spectrum. Arch Dermatol 1975; 111: 1448–52

123. Kulick KB, Provost TT, Reichlin M. Antibodies to single-stranded DNA in patients with discoid lupus erythematosus. Arthritis Rheum 1982; 25: 639–46.

124. Davis P, Atkins B, Hughes GRV. Antibodies to native DNA in discoid lupus erythematosus. Br J Dermatol 1974; 91: 175–81.

125. Elenitsas R, Nousari C H, Seykora J T. Laboratory Methods. In: David E. Elder et al, eds Lever's Histopathology of the Skin. 9th ed. Philadelphia. Lippincott Williams & Wilkins. 2005;(4):64

126. Mimouni D, Nousari CH. Systemic lupus erythematosus and the skin. In: Lahita R., ed. Systemic Lupus Eythematosus, 4th ed. San Diego: Elsevier Science, 2003: Chapter 29.

127. Millard LG, Barker DJ. Development of squamous cell carcinoma in chronic DLE. Clin Exp Dermatol 1978; 3: 161.

128. Fanti PA, Tosti A, Peluso AM et al. Multiple keratoacanthoma in discoid lupus erythematosus. J Am Acad Dermatol 1989; 21: 809–10.

129. Farber JN, Koh HK. Malignant fibrous histiocytoma arising from discoid lupus erythematosus. Arch Dermatol 1988; 124: 114–6.

130. de Berker D, Burge S, Dissaneyeka M. The sequelae of chronic cutaneous lupus erythematosus. Lupus 1992; 1: 181–6.

131. Michelle Petri et al. Derivation and Validation of the Systemic Lupus International Collaborating Clinics Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheum.2012;64(8):2677-86

132. Alsanafi S, Werth VP. Squamous cell carcinomas arising in discoid lupus

erythematosus scars: unusual occurrence in an African-American and in a sun-protected area. J Clin Rheumatol. 2011 Jan;17(1):35-6.

133. JG Harper, MF Pilcher, Squamous cell carcinoma in an African American with discoid lupus erythematosus: a case report and review of the literature. South Med J. 2010 Mar;103(3):256-9

134. Keith W D, Kelly A P, Squamous Cell Carcinoma Arising in Lesions of Discoid Lupus Erythematosus in Black Persons. Arch Dermatol. 1980;116(3):315-317

135. Kern A B,Schiff B L, . Discoid Lupus Erythematosus Following Trauma Report of Cases and Analysis of a Questionnaire.Arch Dermatol. 1957;75(5):685-688

136. Bajaj DR, Devrajani BR et al. Discoid Lupus Erythematosus: A Profile. J Coll Physicians Surg Pak. 2010, Vol. 20 (6): 361-364

137. Tang WYM, Chan LY, Lo KK (1996). Discoid lupus erythematosus in Hongkong Chinese: A review of 12 cases. HKMJ. 2: 239-245.

138. Ng SK, Ratnam KV, Tan T (1985). Discoid lupus erythematosus in Singapore. Singapore Med. J. 26: 365-368.

139. Parish LC, Kennedy RJ, Hurley HJ. Palmar lesions in lupus erythematosus. Arch Dermatol 1967; 96: 273–6.

140. Sandipan Dhar, Kanwar AJ.Discoid lupus Erythematosus in northern India: A study of 102 patients. Ind J Dermatol 1996:41(4):118-121.

141. Wilson C.L., Burge S.M., Dean D. and Dawber R.P.R. Scarring alopecia in discoid lupus erythematosus. Br J Dermatol,1992; 126: 307–314.

142. Looi, L. M. Primary localised cutaneous amyloidosis in Malaysians. Australas J Dermatol,1991; 32: 39–44.

143. Francisco Tausk , Irma Gigli. The Human C3b Receptor: Function and Role in Human Diseases. J Invest Dermatol 1990; 94, 141s–145s

144. F Handa, Radba Rani, Garg K R. Familial Discoid Lupus Erythematosus.IJDVL1973;39(5)213-215

145. Belin DC, Bordwell BJ, et al. Familial discoid lupus erythematosus associated with heterozygote C2 deficiency. Arthritis Rheum. 1980 Aug;23 (8):898-903

146. Karjalainen TK, Tomich CE. A histopathologic study of oral mucosal lupus erythematosus. Oral Surg Oral Med Oral Pathol 1989; 67: 547.

147. Schiodt M, Halberg P, Hentzer B. A clinical study of 32 patients with oral

discoid lupus erythematosus. Int J Oral Surg 1978; 7: 85

148. Callen JP. Oral manifestations of collagen vascular disease. Sem Cutan Med Surg 1997; 16: 323

149. Lee NY, Daniel AS et al. Cutaneous Lupus After Herpes Zoster: Isomorphic, Isotopic, or Both?. Pediatr Dermatol. 2012 May 29.

150. Kathleen M. David-Bajar et al. Clinical, Histologic, and Immunofluorescent Distinctions Between Subacute Cutaneous Lupus Erythematosus and Discoid Lupus Erythematosus. J Invest Dermatol 1992 Sep; 99(3):251-7

151. Antonov D, Kazandjieva J et al.drug-induced lupus Erythematosus.Clin Dermatol.2004;22:157-66.

152. Stratigos AJ et al.Discoid lupus Erythematosus like eruption induced by infliximab.Clin Exp Dermatol.2004;29:150-3

153. Jacobe HT, Sontheimer RD. Autoantibodies Encountered in Patients with Autoimmune Connective Tissue Diseases. In : Bolognia J, et al, eds. Dermatology, 2nd ed., London: Mosby, 2008: 551-2

154. Pittellcow MR, Daould MS. Lichen planus. In: Wolff K, Goldsmith LA, Katz SI, eds. Fitzpatrick's Dermatology in General Medicine, 7th edn. Philadelphia: McGraw-Hill; 2008. p.250.

A clinical study on DISCOID LUPUS ERYTHEMATOSUS

PROFORMA

Case no: Date:

NAME AGE SEX

ADDRESS ph no:

occupation: farmer, Construction worker, Others

AGE AT ONSET OF LESION

DURATION OF LESION

H/O PHOTOSENSTIVITY

H/O ORAL LESION

SYSTEMIC SYMPTOMS

H/O Raynaud's phenomenon , joint pain , dyspnoea , muscle weakness, chest pain, dysphagia, oliguria, visual disturbances, seizures, hair loss,menstrual disturbances,spontaneous or recurrent abortion

TRIGGERING FACTORS

H/O drug intake

H/O fever,preceeding infection

H/O vaccination

H/O UV exposure

H/O trauma

H/O X-Ray Exposure

H/O seasonal variation

H/O smoking

FAMILY H/O:

TYPE-LOCALISED, DISSEMINATED

MORPHOLOGY

1. Classic discoid LE (DLE)
    a. Localized DLE
    b. Generalized DLE
2. Hypertrophic/verrucous DLE
3. Lupus profundus/lupus panniculitis
4. Mucosal DLE
5. Lupus tumidus (urticarial plaque of LE)
6. Chilblain LE (chilblain lupus)
7. Lichenoid DLE (LE/lichen planus overlap, lupus planus)

NUMBER OF LESION: < 5 5-10 >10

SITE& NO:1.head&neck

Scalp

Face-forehead Nose Ear –concha, triangular fossa

cheek perioral lids

2.Disseminated-exposed, unexposed, both

Trunk, upper limbs, lower limbs, palms & soles

NON SPECIFIC LE LESION

MUCOSA- site, pattern

HAIR-

SEQULAE

scarring

pigmentation

cribriform perioral scar

calcification

COMPLICATION

NEOPLASM-SCC

INVESTIGATIONS

COMPLETE HEMOGRAM

URINE ANALYSIS

RFT

LFT

ANA

HPE

DIF

OTHER DISEASE ASSOCIATIONS

PLE, thyroiditis -hypo/hyper , Porphyria, pemphigus, Polychondritis, vitiligo, others.

Risk factors for the development of SLE in patients with DLE:

CLINICAL-

Generalized lymphadenopathy;

SCLE/ACLE skin lesions;

LE-non-specific skin lesions such as vasculitis,

Diffuse non-scarring alopecia,

Periungual nail fold telangiectasia,

Raynaud phenomenon;

LAB-

Unexplained anemia;

Marked leukopenia;

False-positive tests for syphilis;

ANA positivity;

Hypergamma-globulinemia;

ESR (especially > 50 mm/hour);

positive, sun-protected, non-lesional lupus band test (LBT) .

,

KEY TO MASTER CHART

A	-	Anaemia
AHT	-	Antipsychiatry drugs
ATT	-	Anti tuberculous drugs
Alb	-	albuminuria
Bm	-	Buccal mucosa
C	-	Classical discoid lesion
D	-	Disseminated
DP	-	depigmented patch
DNSA	-	diffuse non scarring alopecia
Dis	-	discoid
E	-	Erosion
EP	-	erythematous plaque
F	-	Female
Gin	-	gingiva
HZ	-	Herpes zoster
L	-	Localized
LN	-	lupus nephritis
Lp	-	Lower lip
M	-	Male
Mu	-	Mucosa
MA	-	Macular amyloid
Ma.r	-	Malar rash
Mel	-	melasma
Neg	-	negative
OE	-	oral erosion
P	-	present
Pa	-	Panniculitis

Pal	-	Palate
Pos	-	positive
S	-	satisfied
SA	-	scarring alopecia
SSc	-	Systemic Sclerosis
Sm	-	smoking
T	-	telangiecctasia
TD	-	thyroid dysfunction
Thy	-	thyroxine
Tr	-	trauma
Tu	-	Tumid DLE
V	-	Verrucous DLE
Vo	-	Vitiligo

Ref. No. 00216 /E4/3/2011 Govt.Rajaji Hospital,Madurai.20.
Dated: .01.2012

Institutional Review Board / Independent Ethics Committee.
Dr. A. Edwin Joe, M.D (FM), BL.,
Dean, Madurai Medical College & 2521021 (Secy)
Govt Rajaji Hospital, Madurai 625020.
Convenor
grhethicssecy @gmail.com.

Sub: Establishment-Govt. Rajaji Hospital, aMadurai-20-
Ethics committee-Meeting Agenda-communicated.regarding

The next Ethics Committee meeting of the Govt. Rajaji Hospital, Madurai was held at 11.00 Am to 1.00Pm on 27.01.2012 at the Dean Chamber, Govt. Rajaji Hospital, Madurai. The following members of the committee have been attended the meeting.

1. Dr.N.Vijayasankaran,M.ch(Uro.) 094-430-58793 0452-2584397	Sr.Consultant Urologist Madurai Kidney Centre, Sivagangai Road,Madurai	Chairman
2. Dr.P.K. Muthu Kumarasamy, M.D., 9843050911	Professor & H.O.D of Medical Oncology(Retired)	Member Secretary
3. Dr.I.Meena,MD 094-437-74875	Professor of Physiology, Madurai Medical College	Member
4. Dr. S. Jhamiarasi, M.D (Pharmacol)	Professor of pharmacology	
5.Dr.Moses K.Damel MD(Gen.Medicine) 098-121-56066	Professor of Medicine Madurai Medical College	Member
6.Dr.M.Gobinath,MS(Gen.Surgery) 097-871-50040	Professor of Surgery Madurai Medical College	Member
7.Dr.S. Dilshadh, MD(O&G)	Professor of OP&Gyn Madurai Medical College	Member
8.Dr.S.Vadivel Murugan., M.D, 097-871-50040	Professor of Medicine Madurai Medical College	Member
9.Shri.M.Sridher,B.sc.B.L. 099-949-07400	Advocate, 623-B.II.Floor,East II Cross, K.K.Nagar,Madurai.20.	Member
10.Shri.O.B.D.Bharat,B.sc., 094-437-14162	Businessman Plot No.588, K.K.Nagar,Madurai.20.	Member
11.Shri. S.sivakumar,M.A(Social) Mphil 093-444-84990	Sociologist, Plot No.31 F.F, K.K. Nagar, Madurai	Member

Following Projects were approved by the committee

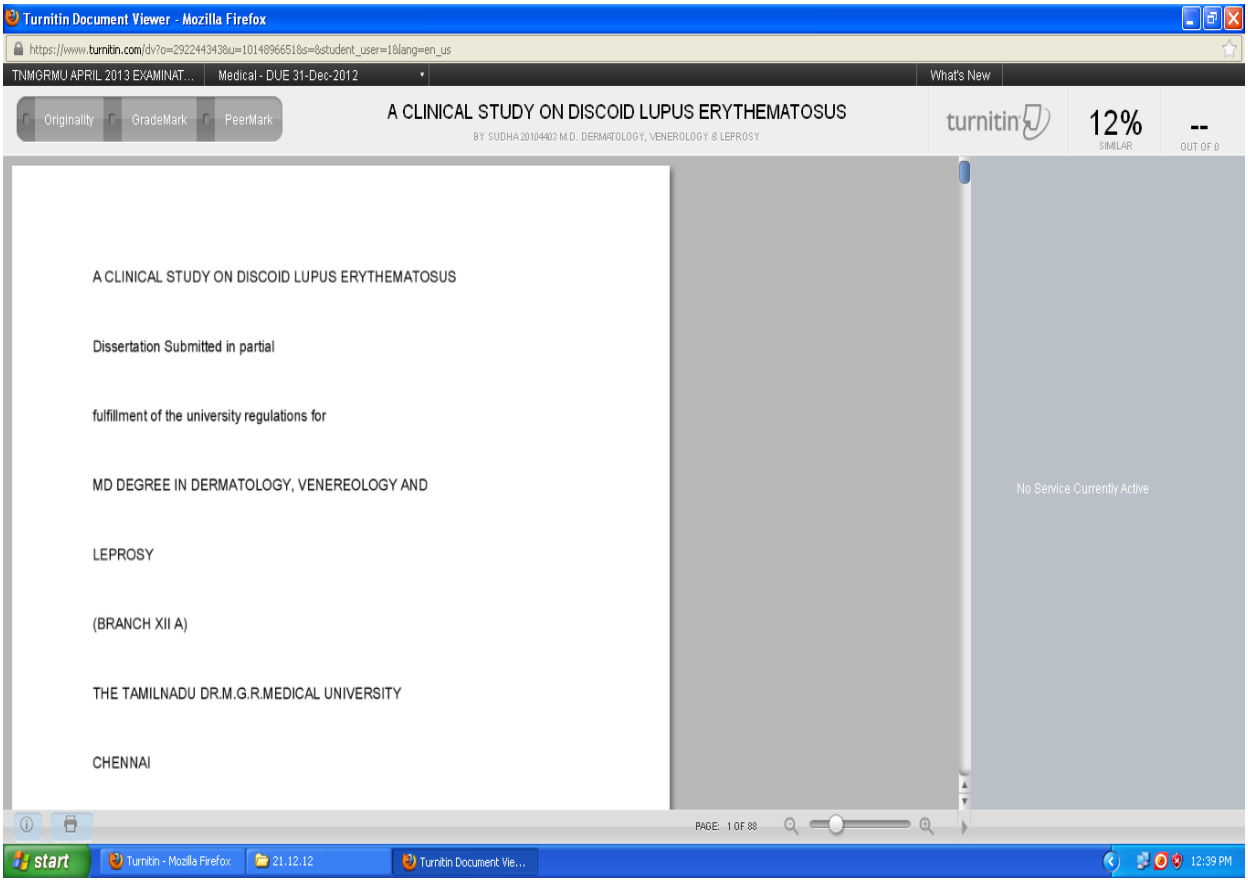
Sl. No	Name of P.G	Course	Name of the Project	Remarks
1.	R. Sudha	PG M.D (dvl)	Discoid lupus erythematosus a clinical study.	Approved

Please note that the investigator should adhere the following. She/He should get a detailed informed consent from the patients/participants and maintain Confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution to Government.
2. She/He should inform the institution Ethical Committee in case of any change of study provedure site and investigation or guide.
3. She/He should not deviate for the area of the work for which applied for Ethical clearance.
She/He should inform the IEC immediately, in case of any adverse events or Serious adverse reactions.
4. She/he should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and apply for if any Extension of time is required She should apply for permission again and do the work.
6. She/He should submit the summary of the work to the Ethical Committee on Completion of the work.
7. She/He should not claim any funds from the institution while doing the word or on completion.
8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

DEAN

To
All the above members and Head of the Departments concerned.
All the Applicants.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MASTER CHART

SLNO	NAME	AGE AT ONSET IN YRS	SEX	DURATION	TRIGGERING FACTORS	TYPE	MORPHOLOGY	NO.OF LESION	SCALP	FOREHEAD	EYELID	NOSE	CHEEK	EAR	PRE AURICULAR	PERIORAL	POST AURICULAR	NECK	TRUNK	UPPER LIMB	LOWER LIMB	PALMS & SOLES	EXPOSED	UNEXPOSED	MUCOSA-SITE	PATTERN	HAIR	HPE	ANA	ASSOCIATION	PHOTOSENSITIVITY	ARTHRALGIA	OTHER LE FEATURES	ARA-CRITERA
1	Maheswari	37	F	2mo	-	L	C	3				P	P										Yes	No				Done		-				
2	Jothibasu	40	M	6mo	-	L	C	1											P				Yes	No				Done	Pos	-				
3	Rajammal	43	F	9yrs	-	L	C,Mu	1											P				Yes	No	Pal	E		Done	Pos	-		P	A,OE	S
4	Pandi	67	M	3yrs	AHT, sm	L	C	1					P										Yes	No				Done	Neg	-	P			
5	Perumayee	43	F	2yrs	Tr	L	C	2	P														Yes	No			SA	Done		-	P			
6	Kalidas	32	M	5yrs	sm	L	C	4	P	P						P							Yes	No			SA	Done		-	P			
7	Sumathy	21	F	5yrs	-	L	C	6				P	P			P							Yes	No				Done		-	P			
8	Jammaal Beevi	42	F	13yrs	AHT	L	C	6	P			P	P	P		P							Yes	No			SA	Done	Neg	-	P			
9	Malathy	27	F	4mo	-	L	C	5				P	P	P									Yes	No				Done	Neg	-	P			
10	Mariammal	55	F	5yrs	AHT,Tr	L	C	5	P				P										Yes	No			SA	Done		-	P		T	
11	Ayyamma	26	F	5mo	-	L	C	2				P	P										Yes	No				Done		-	P			
12	Usharani	39	F	1yr	ATT	L	C	6	P					P									Yes	No			SA	Done	Pos	MA	P		A	S
13	Pitchaii ammal	53	F	I1/2yrs	ATT	L	C	2						P					P				Yes	No				Done	Pos	-	P	P		
14	Ramayee	59	F	1yr	AHT	L	C	6	P								P						Yes	No			SA	Done		-	P	P		
15	Kamatchi	42	F	3yrs	-	L	C	5	P							P							Yes	No			SA	Done		-	P	P		
16	Shanthi	39	F	6mo	-	L	C	3	P	P													Yes	No			SA	Done	Neg	H	P			
17	Virumayee	38	F	12yrs	-	L	C	1	P														Yes	No			SA	Done		PLE	P			
18	Shanthi	39	F	3yrs	thy	L	C,Mu	4	P			P											Yes	No	Lp	Dis		Done		TD		P		
19	Karuppi	43	F	7yrs	-	L	C,Mu	4									P						Yes	No	Lp	Dis		Done		-	P			
20	Gulzar banu	40	F	3mo	-	L	C,Mu	5						P	P								Yes	No	Lp	Dis		Done	Neg	Mel				
21	Gandhimathi	23	F	1mo	-	L	C,Mu	2				P											Yes	No	Lp	Dis		Done		-	P			
22	Poovandhi	39	F	1yr	-	L	C,Mu	5			P	P	P										Yes	No	Lp	Dis		Done	Neg	-	P			
23	Natchi	34	F	1yr	-	L	C,Mu	6	P	P	P				P								Yes	No	Up,Lp	Dis	SA	Done	Pos	TD	P	P		
24	Meenatchi	22	F	1yr	thy	L	C,Mu	4				P	P										Yes	No	Up,Lp	Dis		Done	Neg	TD	P	P		
25	Pitchaiammal	55	F	1mo	-	L	C,Mu	3											P				Yes	No	Lp	Chei		Done	Pos	TD	P		Alb	S
26	Petchiammal	31	F	6mo	-	L	C,Tu,Mu	6				P	P	P									Yes	No	Up	Dis		Done		-	P			
27	Sakila	36	F	2yrs	herpes	L	C,Mu	1					P										Yes	No	Lp	Dis		Done		-				
28	Pitchaiammal	30	F	5yrs	-	L	C,Mu	2							P								Yes	No	Up,Lp	Dis		Done		-	P			
29	Chellamani	47	F	2yrs	-	L	Tu	1				P											Yes	No				Done	Pos	Mel		P		
30	Kuruvammal	68	F	2yrs	-	L	V	4													P		No	Yes				Done		-				
31	Chandra	41	F	4mo	-	D	C	>10	P	P			P					P	P	P			Yes	No				Done		-	P			
32	Vellaiyammal	42	F	8yrs	-	D	C	5	P					P					P	P			Yes	No			DNSA	Done	Pos	SSc,Vo,TD	P			
33	Sundarrajan	45	M	2yrs	sm	D	C	>10	P	P				P					P	P			Yes	Yes			SA	Done	Pos	familial	P			
34	Balasubramaniam	37	M	3yrs	-	D	C,Mu	>10	P				P	P					P	P	P		Yes	Yes	Bm,gin	DP	SA	Done	Pos	TD	P	P	A	S
35	Viji	27	F	2mo	varicella	D	C	>10					P	P					P	P			Yes	No			DNSA	Done	Pos	-	P	P		
36	Chitra	26	F	12yrs	-	D	C	4	P	P									P				Yes	Yes			SA	Done	Pos	-	P	P	Ma.r	S
37	Bothaguru	41	M	6yrs	APT,sm	D	C,Mu	>10		P		P		P				P	P	P			Yes	No	Lp	Dis		Done		-				
38	Selvam	39	M	2mo	sm	D	C,Mu	8	P			P	P	P				P	P				Yes	No	Up,Lp,Bm	Dis,EP	SA	Done		-	P			
39	Amirtham	40	F	20yrs	-	D	C,Mu	>10		P			P						P	P			Yes	No	Lp	Dis		Done	Pos	-	P			
40	Savithiri	25	F	13yrs	-	D	C,Mu	>10	P										P	P	P		Yes	Yes	Pal	E	SA	Done	Pos	-	P	P	A,OE	S
41	Veerammal	37	F	1yr	-	D	C,Mu	>10						P					P	P			Yes	No	Lp	Dis		Done	Pos	-	P	P	SCLE	
42	Malarvizhi	37	F	4yrs	ATT	D	C,Mu	>10		P									P	P	P	P	Yes	Yes	Up,Lp	Dis	DNSA	Done	Pos	PT	P	P		
43	Kamala	40	F	6yrs	-	D	C,Mu	>10	P	P				P					P	P			Yes	Yes	Up,Lp	Dis	SA	Done	Pos	-	P		Alb	S

44	Veerakal	14	F	6mo	Burns	D	C,Mu	>10	P								P		P	P			Yes	Yes	Up,Lp	Dis		Done		-	P	P		
45	Palaniyammal	41	F	I yr	-	D	C,Mu	>10	P	P	_	_	_	P	_	_	_	_	P	P	_	_	Yes	No	Up,Lp	Dis	_	Done	Pos	-	P	P	Ma.r	S
46	Pillapan	38	M	10yrs	sm	D	C,Mu,V	8	P	_	_	P	P	P	_	_	_	_	P	P	_	_	Yes	Yes	Lp	Dis	SA	Done	Pos	TD,HZ,	P	P	SCLE,A,LN,alb	S
47	Raja	42	M	4yrs	sm	D	C,Mu,V	>10	P	_	_	P	P	_	_	_	_	_	P	P	P	P	Yes	Yes	Lp,Pal,Bm,gin	Dis,DP	SA	Done	Pos	-	P	P	A	S
48	Jyoti	15	F	8mo	Trauma	D	C,Pa	4	P	P	_	_	P	P	_	_	_	_	_	P	_	_	Yes	Yes	_	_	SA	Done	Pos	-	P	_	_	_
49	Palanisamy	40	M	20yrs	sm	D	C,V	>10	P	_	_	_	_	P	_	_	_	_	P	P	P	P	Yes	Yes	_	_	_	Done	Pos	H	P	P	A	S
50	Glory	25	F	5yrs	-	D	C,Mu	>10	P	P	_	_	_	_	_	_	_	_	P	P	P	_	Yes	Yes	Up,Lp	Dis	SA	Done	_	-	P	_	A	S
51	Selvi	26	F	2yrs	-	D	Pa	8	_	_	_	_	P	_	_	_	_	_	_	P	P	_	Yes	Yes	_	_	_	Done	Neg	-	_	P	_	_